Characterisation of in-hospital complications associated with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol UK

Characterisation of in-hospital complications associated with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol UK: A prospective, multicentre cohort study.

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Evidence before this study

Data from other areas of healthcare, such as surgery, suggest COVID-19 patients are at greater risk of subsequent complications, but systematic characterisation of complications in COVID-19 patients has not yet been undertaken. At present, most COVID-19 studies have focused on mortality and respiratory support outcomes. Characterising the burden of complications is important for healthcare system preparedness for further waves of infection, determining future population morbidity, understanding the full repercussions of COVID-19 for society, and for informing future research and clinical guidelines. The current literature is comprised of several small cohort or case-control studies which focus on specific organ systems or conditions. There is a lack of prospective systematically collected data describing the in-hospital complications of COVID-19.

Added value of this study

Hospitalised adult patients with COVID-19 frequently had complications, even in younger age groups and in those with few pre-existing comorbidities. Occurrence of complications was associated with a significantly reduced ability to self-care at discharge, which was seen in all age and comorbidity groups. While patients under the age of 50 years are at low risk of dying, we found high rates of complications across all age groups.

Implications of all the available evidence

In patients admitted to hospital with COVID-19, there is a burden of immediate complications affecting all age groups. Many of the complications identified are likely to have important long-term effects. Healthcare systems and policy makers should prepare for increases in population morbidity arising from COVID-19 and its subsequent complications. As complications following COVID-19 are common across all age groups and comorbidities, public health messaging around the risk COVID-19 poses to younger otherwise healthy people should be considered alongside vaccine prioritisation. Further studies are required to understand the medium to long-term effects of COVID-19 and how immediate complications may lead to lasting morbidity.

Abstract

Background

COVID-19 is a multi-system disease and patients who survive may experience in-hospital complications. These complications are likely to have important short and long-term consequences for patients, healthcare utilisation, healthcare system preparedness, and society amidst the ongoing COVID-19 pandemic. Our aim was to characterise the extent and impact of COVID-19 complications, particularly in those who survive using the International Severe Acute Respiratory and emerging Infections Consortium (ISARIC) WHO Clinical Characterisation Protocol UK (CCP-UK).

Methods

A multicentre, prospective cohort study in 302 UK healthcare facilities of adults hospitalised with COVID-19 between 17th January and 4th August 2020. Complications were defined as organ specific diagnoses occurring alone or in addition to any hallmarks of COVID-19 illness. Outcomes included death, critical care use, and ability to self-care at hospital discharge. We used multilevel logistic regression and survival models to explore associations between these outcomes and in-hospital complications, age, and pre-existing comorbidities.

Results

Of patients admitted to hospital for management of COVID-19, 49.7% (36 367/73 197) experienced at least one complication. The mean age of our cohort was 71.1 years old (SD 18.7), included more males (56.0%, 41 025/73) with 81.0% (59 289/73 197) of patients having at least one comorbidity. Males over 60 were most likely to experience a complication (60 y and over, 54.5% [16 579/30 416] in males and 48.2% [11 707/24 288] in females; Under 60 y, 48.8% [5179/10 609] in males, 36.6% [2814/7689] in females). Renal (24.3%, 17 752/73 197), complex respiratory 18.4% (13 486/73 197), and systemic (16.3%, 11 895/73 197) complications were most frequent. Cardiovascular (12.3%, 8973/73 197), neurological (4.3%, 3115/73 197), and gastrointestinal/liver (0.8%, 7901/73 197) complications were also reported. The presence of any complication was associated with significantly worse survival (adjusted HR 1.74, 95% CI 1.64 to 1.84) and increased admission to critical care (adjusted OR 7.25, 95% CI 6.83 to 7.69). Reduced ability to self-care at discharge was significantly greater in patients who experienced a complication (adjusted OR 2.42, 95% CI 2.31 to 2.54) and was greatest in those who experienced neurological complications (adjusted OR 4.39, 95% CI 3.95 to 4.89).

Conclusions

Complications and worse functional outcomes in patients admitted to hospital with COVID-19 are high, even in young, previously healthy individuals. Acute complications are associated with reduced ability to self-care at discharge, with neurological complications being associated with the worst functional outcomes. COVID-19 complications are likely to cause significant strain on health and social care in the coming years. These data will help in the design and provision of services aimed at the post-hospitalisation care of patients with COVID-19.

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Introduction

Many people across the world have been hospitalised with coronavirus disease 2019 (COVID-19) following infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Current evidence has established these patients have high mortality rates (26%) and up to 17% of patients admitted to hospital will require ventilatory support and critical care[1]. Several case reports, cross-sectional, and case-control studies have described the presence of non-respiratory complications in COVID-19 and suggest that these are likely to be associated with poor outcomes[2–4].

Understanding the possible complications of COVID-19 is important for patient management and for provision in healthcare systems. For patients, information around in-hospital complication rates are important for decision making about treatment, long-term planning, possible resumption of normal activity and, more recently, vaccination. For healthcare systems, these data are vital to inform immediate preparedness measures (i.e., allocation of resources, equipment, and staffing) but also for long-term planning of healthcare delivery to a population which may have incurred additional morbidity due to COVID-19.

A substantial proportion of patients with COVID-19 go on to develop critical illness and require organ support. It is widely recognised that survival following critical illness is accompanied by a significant burden of additional physical and mental health morbidity, which mortality outcomes cannot measure[5,6]. Mortality has been widely used as an outcome in epidemiological studies and randomised controlled trials studying patients with SARS-CoV-2,but fails to capture the immediate short-term health issues experienced by survivors, including in-hospital complications and functional outcomes. In patients with COVID-19 undergoing surgery, high rates of post procedural mortality and complications have been noted, but systematic characterisation of hospitalised patients with COVID-19 is lacking[7]. In other non-SARS-CoV-2 viral illnesses, for example influenza, short-term complications such as myocardial infarction, acute kidney injury (AKI) and stroke, are common and may cause greater morbidity than the initial infection itself[6,8–11]. Understanding who develops short-term complications may also allow clinicians and researchers to develop care pathways and interventions to mitigate the impact of complications.

As many patients with COVID-19 are critically unwell, identifying the burden of short-term morbidity may be useful to understand the long-term burden on healthcare systems and the society for those who survive COVID-19.

We have previously characterised the clinical features of patients admitted to hospital with COVID-19 using the International Severe Acute Respiratory and emerging Infections Consortium (ISARIC) WHO Clinical Characterisation Protocol UK (CCP-UK) for Severe Emerging Infections. The aim of this study was to describe the short-term complications, beyond those associated with the presenting features of COVID-19 and severe acute respiratory infection.

Methods

The ISARIC WHO CCP-UK protocol was developed by international consensus in 2012-14 and activated in response to the SARS-CoV-2 pandemic on 17th January 2020[12]. This is an actively recruiting prospective cohort study recruiting across the United Kingdom. Study materials including protocol, revision history, case report forms, study information and consent forms, are available online[13]. Ethical approval was given by the South Central - Oxford C Research Ethics Committee in England (Ref: 13/SC/0149) and by the Scotland A Research Ethics Committee (Ref: 20/SS/0028). The study is reported in line with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[14].

Adult patients aged 19 years and over, who were admitted to hospital between 17th January 2020 to 4th August 2020 with confirmed or highly suspected SARS-CoV-2 infection leading to COVID-19 were included in this analysis; overall study recruitment is ongoing. We used this WHO age cut-off[15] as children exhibit other patterns of complications including the Multisystem Inflammatory Syndrome. Confirmation of SARS-CoV-2 was performed using reverse-transcriptase polymerase chain reaction (RT-PCR). Highly suspected cases were eligible for inclusion, given that SARS-CoV-2 was an emergent pathogen at time of protocol activation and laboratory confirmation was dependent on local availability of testing.

Data collected by research nurses and volunteer medical students were entered into a standardised electronic case report form within a secure Research Electronic Data Capture (REDCap) database[16]. Multiple timepoints were captured, including admission, hospital stay days 1, 3, 9 and discharge or status at 28 days if not discharged. Data were collected according to a detailed protocol, which was updated to reflect developments over the course of the pandemic. Participant characteristics including age, sex at birth, physiological parameters at presentation and comorbidities were also recorded. Comorbidities included asthma, chronic cardiac disease, chronic haematologic disease, chronic kidney disease, chronic neurological disease, chronic pulmonary disease, HIV/AIDS, history of malignancy, liver disease, clinician-defined obesity, rheumatologic disorders and smoking. Deprivation was calculated by mapping individual postcodes to their corresponding Index of Multiple Deprivation (IMD) using Office for National Statistics (ONS) postcode data. Using national data, we calculated deprivation quintiles, with the first quintile being least deprived and the fifth quintile the most deprived. For patients where postcodes were missing, the average IMD rank, weighted by population in each lower super output area for a given hospital catchment area was used.

Variable definitions

The primary outcome of this study was the incidence of in-hospital complications, defined as organ specific diagnoses occurring alone or in addition to any hallmarks of COVID-19 illness (definitions in supplement pp 1). All complications were recorded so total morbidity could be described, not just those directly attributable to COVID-19. Although COVID-19 is a multisystem disease, severe respiratory infection was considered characteristic of COVID-19 and was not regarded as a complication. Data were collected on organ-specific complications including complex respiratory (bacterial pneumonia, acute respiratory distress syndrome (ARDS), empyema, pneumothorax, pleural effusion), neurological (meningitis, encephalitis, seizure, stroke), cardiovascular (thromboembolism, heart failure, myocarditis, endocarditis, arrhythmia, cardiomyopathy, myocardial ischaemia, cardiac arrest), acute kidney injury, gastrointestinal (acute liver injury, pancreatitis, gastrointestinal haemorrhage) and other systemic complications (coagulopathy, disseminated intravascular coagulation, anaemia, bloodstream infection. The occurrence of complications was determined from routine clinical records by local investigators with the exceptions of bloodstream infection (BSI) and microbiologically confirmed bacterial pneumonia. These were defined based on recorded results from sputum, deep respiratory or blood cultures and restricted to instances where clinically significant organisms were detected in the sample. Blood stream infection was defined as growth of clinically significant bacteria (excluding coagulase-negative Staphylococci) or fungus recorded from blood culture or PCR of blood. Results considered to represent contamination or colonisation were excluded. Owing to the difficulties of obtaining lower respiratory tract samples to confirm bacterial pneumonia and the low positivity rates, we present both highly likely and suspected bacterial pneumonia in supplementary tables.

The existence of likely ARDS was described clinically or defined as one of the following combinations: receiving extracorporeal membrane oxygenation, being nursed in a prone position and receiving invasive mechanical ventilation, receiving mechanical ventilation and having a PF (PaO2 (mmHg) / FiO2) ratio of 300 or less. For acute kidney injury and acute liver injury, we used laboratory measurements with internationally recognised grading systems to detect complications that may have been missed. Acute kidney injury was defined as a creatinine rise which corresponded to Kidney Disease Improving Global Outcomes (KDIGO) stage I or above definition[17] (creatinine rise ≥1.5x baseline value or by ≥26.5 μmol/L). We did not incorporate urine output into this definition, as this parameter is not universally recorded for all patients, particularly

out-with critical care. Acute liver injury was defined as an international normalised ratio (INR) rise of 2.5 times or greater than the lowest entered value, or an INR of over 4.5 (in the absence of warfarin therapy), or an alanine aminotransferase (ALT) rise of greater than 10 times the lowest value, or an ALT over 150, or a bilirubin rise of greater than 15 or a bilirubin greater than 55 (in the absence of any pre-existing liver disease). In those who survived we also captured information on whether self-care ability was the same or worse than before hospital admission at time of discharge, defined clinically as the change in support required before and after hospital admission. For this outcome, if patients required ongoing hospital care, we defined this outcome as 'worse than before onset of COVID-19 illness' due to these ongoing care requirements.

Statistical analysis

Continuous data are presented as a mean with standard deviation (SD) where data are normally distributed and as a median with the 25th and 75th centiles for non-parametric data. Categorical data are summarised as frequencies and percentages. Differences between groups for continuous normally distributed data, were tested using Welch's T-test for two groups or analysis of variance (ANOVA) when there were more than two groups. Non-parametric continuous data were tested using a Mann-Whitney U test for two groups or Kruskall-Wallis test for three or more groups. Differences across categorical data were tested using the Chi-squared test or Fisher's exact test when expected cell counts were less than five. Analysis of complication co-occurrence was done using the Jaccard similarity index and represented visually as heatmaps with dendrograms constructed from complete hierarchical clustering results. We only included patients who had completed outcomes, with at least 2 months of follow-up. There were low rates of missing data and therefore multiple imputation was not used.

To explore if the number of complications and which specific complications were associated with mortality (dependent variable), complication variables were entered independently into Cox Proportional Hazards models and adjusted for other potentially confounding factors. These data were described using Kaplan-Meier plots and modelled using Cox Proportional Hazards regression. Reported date of symptom onset was taken as day zero. Discharge from hospital was considered an absorbing state (once discharged, patients were considered no longer at risk of death), thus discharge did not compete with death. The proportional hazards assumption was checked.

To see whether complications were associated with increased severity of initial disease, we used the 4C Mortality Score, quick sequential organ failure assessment (qSOFA) and National Early Warning Score 2 (NEWS2) on admission or time of symptom start to examine the relationship between severity and presence of any in-hospital complications[18]. These scores are commonly used in clinical practice to identify patients with deteriorating or critical illness and risk of subsequent death in general adult hospital populations (NEWS2 and qSOFA) or in COVID-19 patients (4C Mortality Score). We calculated the score for each adult patient in the dataset and plotted each score against the observed incidence of complications in each score group.

Multilevel logistic regression models were constructed to identify associations between patient characteristics (potential confounders including patient demographics and existing comorbidities) and the development of specific complications, the worse self-care ability on discharge, and the requirement for ongoing hospital care. For all models, variable selection was performed based on clinical plausibility, and final models were selected based on clinical relevance guided by minimisation of the Akaike information criterion (AIC). Centre-level variation was accounted for using mixed-effects models which included hospital as a random effect and patient-level variables as fixed effects. We conducted stratified analyses to focus on survivors and on those admitted to critical care.

To identify which patient groups are at the highest risk of complications and mortality, we used generalised additive models and generated risk estimates by age, sex and comorbidity status. Generalised additive models accommodated potential nonlinear relationships between variables with the inclusion of penalised thin-plate regression splines on continuous variables. We did this for each organ-specific complication outcome, as well as testing the associations between organ-specific complications and death. Models were adjusted for age, sex, comorbidity status and deprivation (IMD quintile). First- and second-order interactions where they significantly contributed to model fitting. We ran 100 bootstrap replicates for each model to provide a visual representation of the distribution.

All statistical analyses were performed using R version 3.6.3 (R Foundation for Statistical Computing, Vienna, AUT) with the tidyverse, finalfit, mcgv, survival, stringdist, janitor and Hmisc packages.

Role of the funding source

The study sponsors and funders had no role in the study design, collection, analysis, data interpretation or report writing. TMD, AMR, RP, JKB, ABD, MGS and EMH had access to the raw data. The corresponding author had full access to all data and the final responsibility to submit for publication.

Results

Included patients

As of 4th August 2020, 80 388 patients were included in the CCP-UK study (figure 1). Of these, 75 276 were adults aged 19 years or over, 97.2% (73 197/75 276) had any complication outcome available for analysis. The overall mortality rate was 31.5% (23 092/73 197), and the overall complication rate was 49.7% (36 367/73 197 experienced at least one complication). In surviving patients, 43.5% (21 784/50 105) experienced at least one complication. Proportions of patients experiencing at least one complication were highest in age groups over 60 (table 1). Missing data for each variable were under 10% for nearly all patient characteristics included in the study (shown in supplement pp 3-4). Out of all patients included, 85.9% (62 894/73 197) had a positive SARS-CoV-2 PCR test. Patients who did not have a positive swab had the same or slightly lower rates of complications overall and organ-specific complications (supplement pp 3).

Patient demographics

The mean age of patients included in our study was 71.1 years old (SD 18.7), with the majority of those included being male (56.0%, 41 025/73 197, Table 1). One or more comorbidities were present in 81.0% (59 289/73 197) of the cohort. Chronic cardiac disease was the most common comorbidity (30.8%, 22 563/73 197), followed by chronic pulmonary disease (16.7%, 12 235/73 197) and chronic kidney disease (16.6%, 12 182/73 197). Most patients were of a white ethnicity (73.5%, 53 780/73 197).

Incidence and patterns of complications

In adult patients with COVID-19, renal (24.3%, 17 752/73 197), complex respiratory 18.4% (13 486/73 197), cardiovascular 12.3% (8973/73 197), neurological 4.3% (3115/73 197), gastrointestinal (including liver) 10.8% (7901/73 197) and systemic complications 16.3% (11 895/73 197) were reported (table 1). Specific complications within each organ system were also reported, with AKI, likely ARDS, liver injury, anaemia and cardiac arrhythmia most common (supplement pp 4-5). The incidence of AKI increased with age and was most common in patients aged between 60 and 90 years of age, with males at greater risk. Patients with chronic kidney disease were at the highest risk of AKI, with 39.8% developing AKI (4785/12 182) versus 21.6% (11 962/55 458) in patients without chronic kidney disease. Cardiac complications increased with age and in patients with existing cardiac disease. In those with existing cardiac disease, 19.9% (4496/22 563) developed a cardiac complication compared to 8.9% (4077/45 563) in those without previous cardiac disease. In contrast, liver injury was most frequently seen in younger age groups

under 60 years old, with the highest rates occurring in males. Liver injury was more common in patients with pre-existing moderate/severe liver disease (22.4%, 300/1340) compared to those without (6.2%, 4097/65 646). Complication rates were comparable across white, South Asian and East Asian ethnicity groups, but were highest in those of black ethnicity (57.8% 1433/2480 compared to 49.1% 26 431/53 780 in white, table 1). Rates of acute kidney injury were highest in black patients (33.1% 822/2480, compared to 24.0% in white patients 12 896/53 780). Obese patients were 1.6 times more likely to have respiratory complications (28.1%, 2059/7329 in obese versus 17.8%, 9498/53 415 in non-obese) and 1.3 times more likely to have renal complications (30.1%, 2208/7329 in obese versus 23.7%, 12 656/53 415 in non-obese, table 1).

Suspected bacterial pneumonia was the most common respiratory complication (supplement pp 6-7), but when the definition incorporated positive microbiological testing (highly likely bacterial pneumonia), the incidence of highly likely bacterial pneumonia was lower. Acute kidney injury (Jaccard index 0.23), likely ARDS (Jaccard index 0.17), anaemia (Jaccard index 0.13) and liver injury (Jaccard index 0.10) were most likely to co-occur with death (heatmap for all in supplement pp 35).

Predictors of developing complications

Experiencing at least one complication was common across all demographic groups, with the lowest rates in patients aged 19 to 29 with no comorbidity (21.2%, 178/839) and highest in the 60 to 69 age group in patients with two or more comorbidities (57.9%, 3340/5767; supplement pp 8-11). The incidence of complications rose with increasing age occurring in 38.9% (3 596/9 249) in those aged 19 to 50 years and 51.3% (32 771/63 948, figure 2A) in those aged 50 years and older. The number of complications increased with number of pre-existing comorbidities, particularly in older individuals (figure 2A, supplement pp 8-11). Complications were higher in males compared with females, and although males were more likely to experience complications at younger ages, males over 60 were most likely to experience a complication (aged under 60, 36.6% [2814/7689] in females and 48.8% [5179/10 609] in males; aged 60 and over, 48.2% [11 707/24 288] in females and 54.5% [16 579/30 416] in males; figure 2A; supplement pp 4-5). Young males without comorbidities were significantly more likely to experience complications than females without comorbidities (28.4% [94/331] in males aged 19 to 29 and 16.6% [84/505] in females aged 19 to 29; figure 2A). When we stratified by mortality, complications occurred more frequently patients who died (63.2%, 14 583/23 092), but were still commonly experienced by

survivors (43.5%, 21 784/50 105, supplement pp 12-13) and there were direct relationships between worse survival and increasing numbers of complications (figure 2B).

After adjusting for age, sex, deprivation, comorbidities and centre, increasing age and male sex were significant independent predictors for developing any complication and for all organ specific complications except for gastrointestinal and liver complications, which younger patients were more likely to experience (figure 3A, supplement pp 36-44). Those with pre-existing comorbidities that affected a specific organ system were at higher risk of developing a complication affecting the same organ (supplement pp 45-46). The relationship between increasing age, male sex and the risk of complications persisted independent of the number of comorbidities (figure 3A, supplement pp 39-44). The risk of complications and relationship between age and risk of complications were comparable across all comorbidity groups.

Survival and in-hospital complications

In patients who survived to 28 days from first symptoms to discharge, 44.9% (23 619/52 582) suffered complications, compared with 61.9% (12 624/ 20 384) in those who died within 28 days. Complications were more common in those requiring respiratory support and were highest in patients who received critical care (82.4%, 8267/10 034), or who received invasive mechanical ventilation (91.7%, 5619/6122, table 2). The presence and number of complications was significantly associated with worse in-hospital survival (figure 2B). Following adjustment for age, sex, deprivation, and hospital, the occurrence of any complication was significantly associated with poorer overall survival (figure 2C). Cardiovascular (HR 1.98, 95%CI 1.85 to 2.11) and complex respiratory complications (HR 2.15, 95%CI 2.04 to 2.27) were most strongly associated with worse outcomes. After adjustment for age, sex and deprivation, patients experiencing an acute kidney injury were 4 times more likely to be admitted to critical care and those with respiratory complications were 13 times more likely to be admitted to critical care (figure 2D).

When the relationships between complications and mortality were modelled using generalised additive models and plotted (figure 3B, supplement pp 39-44), the presence of any complication, in addition to increasing age and male sex was associated with death. In younger people, complications were associated with a greater risk of mortality compared to individuals of the same age, than in older people. Associations between complications and mortality were similar across comorbidity groups overall, but we identified that in younger people with comorbidities, mortality was much higher in those who experienced complications compared to people of the same age

without complications. Respiratory and cardiovascular complications were associated with the largest increases in death across all ages, whereas those with neurological or systemic complications were most likely to survive (supplement pp 39-44).

Severity and symptoms

Physiology-based early warning scores and the 4C Mortality Score using parameters at hospital admission, were associated with the occurrence of complications in survivors. Higher 4C Mortality Score on admission corresponded with an increased probability of at least one complication (supplementary figure 13A, supplement pp 47). Similarly, higher NEWS2 (supplementary figure 13B, supplement pp 47) and qSOFA scores on admission (supplementary figure 13C, supplement pp 47) were associated with an increased probability of one or more complications. The number of symptoms on admission did not appear to be related to the incidence of complications (supplementary figure 13D, supplement pp 47).

Functional outcomes in COVID-19 survivors

In those who survived, 26.6% (13 309/50 105) of patients had worse ability to self-care than they did prior to their illness (figure 4A). This increased with age, male sex and in those who received critical care support (figure 4A and 4B). Experiencing a complication was independently associated with an increased risk of worse ability to self-care after discharge after adjusting for age, sex, deprivation, and hospital (adjusted OR 2.42, 95% CI 2.31 to 2.54, figure 4C). Neurological complications had the strongest associations with worse functional outcome (adjusted OR 4.39, 95% CI 3.95 to 4.63, figure 4C).

Discussion

Hospitalisation with COVID-19 is associated with high rates of morbidity in adults. Almost half of survivors had one or more complications, which were more likely in patients who required critical care. Survivors of COVID-19 who had suffered at least one complication had a lower ability to self-care on discharge from hospital. The effect of complications on the ability to self-care was most profound in younger patients under the age of 50 years. We found that complication rates were high in every age group and increased with age. Unlike mortality, there were only small differences in complication rates in groups stratified by pre-existing comorbidity. Males were significantly more likely to develop complications than females.

The most common complications in our data were acute kidney injury, complex respiratory and systemic complications. Although our study only looked at complications during the first admission for COVID-19, many of the common complications identified are associated with significant long-term morbidity. Acute kidney injury is known to be associated with increased long-term hazards of mortality, requirement for dialysis and an increase in cardiovascular events[19–21]. In addition to the more common complications identified, rarer complications including stroke, congestive heart failure and cardiac arrest were present in 1 to 5% of patients[22–24]. Patients who received critical care had the highest complication rates, compatible with previous observations describing high levels of morbidity in those who require critical care[6,8,25,26]. The least commonly observed were neurological complications, although these were the most strongly associated with reduced ability to self-care. Suspected bacterial pneumonia and likely ARDS were the most common respiratory complications. When compared with the published literature on influenza, complications rates in patients with COVID-19 were the same or higher[27–29]. Interestingly, this appears to be primarily driven by non-infectious complications, as the rates of secondary bacterial infection in patients with COVID-19 were lower than described in influenza[30]. Notably, COVID-19 patients had up to 19 times the risk of developing likely ARDS when compared to patients admitted with influenza[31].

Most clinical studies of COVID-19 have focussed on associated mortality[1]. Mortality is a hard endpoint, relatively easily measured, and of utmost importance. However, its use as a sole outcome in COVID-19 studies may underestimate the detrimental impact of COVID-19, particularly in those who are younger or otherwise healthy. Our analysis suggests that the odds of some complications change little with increasing age for patients aged over 50 years, and is an effect not just confined to the elderly. Similarly, our data show only small increases in risk of complications by pre-existing comorbidities. The effect of comorbidities on the risk of

complications and death was significantly higher in younger people compared with people without comorbidities of the same age. We also observed the differences in number of complications decrease between those who died and those who survived as age increased, suggesting that although young people are less likely to die, they may be proportionally more likely to survive and live with complications. Patients with complications are also likely to have impaired ability to self-care following discharge from hospital. This contradicts current narratives that COVID-19 is only dangerous in people with existing comorbidity and the elderly. Dispelling and contributing to the scientific debate around such narratives has become increasingly important. Many countries including the UK are experiencing further waves of infection[32]. Suggestions have been made around using younger, healthy demographic groups who are less likely to die, to help support economic output, and to propagate herd immunity within a population[33]. Policy makers need to ensure that regarding any groups as 'low-risk', based on a lower likelihood of mortality at a population level, may not fully account for the in-hospital and longer-term consequences these patients may face.

Our data provide the most comprehensive analysis to date of the impact of COVID-19 on short-term clinical outcomes in a hospitalised population. Data were collected prospectively and capture the majority of people hospitalised with COVID-19 in the UK. Recruitment to our study continues, enabling us to capture trends and incidence of complications in near real-time. Other smaller, or single centre studies, have typically focussed either exclusively on patients who received critical care, or on one type of complication and lack systematic approaches to data collection[4,34–38]. Our study identifies high rates of complications and the risk factors for developing these, and describes severity, which previous studies have been unable to do at scale. In particular, we find that in the short-term, respiratory and cardiovascular complications have the strongest association with mortality. A further strength is our study includes patients in both critical care and in ward-level areas, whereas other groups have just studied intensive care populations[39]. In addition, the multicentre nature of our study across 302 facilities in four countries increases the generalisability of our findings, which is particularly important to provide robust estimates of short-term morbidity for healthcare planners and policy makers. The large sample size of our study allowed us to conduct meaningful subgroup analyses and integrate blood test and microbiology results to increase robustness. This size also meant we could detect rare events in important patient groups such as those receiving critical care, younger patients, and survivors where complications may have the biggest impact and be with patients for a long period of time after the initial event.

This study has important implications for clinicians. It was not possible for us to causally link complications and consequent poor outcomes. However, it is plausible that interventions targeted at preventing in-hospital complications or reducing their impact could plausibly improve outcomes. We found respiratory and cardiovascular complications were associated with greatest severity and acute kidney injury was one of the most common. Treatments such as enhanced monitoring and early treatment for patients for cardiac arrhythmias which may lead to further problems such as stroke or cardiac arrest may be therefore useful. Similarly, for acute kidney injury optimising fluid balance to ensure adequate renal perfusion in patients with less severe respiratory disease may lessen the impact of AKI. Our data also present research opportunities for preventing complications that contribute to significant disability. For example, further characterisation of thromboembolic complications and stroke may help to identify optimal anticoagulation strategies in patients with COVID-19[40]. We found initial disease severity, measured using the 4C Mortality Score, qSOFA and NEWS, were associated with the presence of complications, and could therefore be useful tools to stratify those at the highest risk of developing complications in clinical practice and interventional trials.

There are several limitations to our study, which relate to the design and current unknowns in COVID-19 research. Firstly, this dataset focusses on in-hospital complications during the index admission for COVID-19 and does not provide longer-term outcome data or data on quality of life. Nevertheless, our results suggest that complications of COVID-19 may affect all survivor groups, rather than just those who are older and have comorbidities. Secondly, the complications that were captured were predefined by a pragmatic outbreak preparedness study protocol, and case report form developed for “Disease X”, and long before the emergence of SARS-CoV-2. The outcomes we chose are both clinically important and associated with complications observed in other infectious viral diseases. Local investigators could enter other complications as free text, but this approach may have missed some important outcomes which were otherwise unexpected (i.e. venous thromboembolism); however, as these emerged we amended the case report form to include these. This suggests our estimates are likely to be conservative, when compared to the incidence of some complications (including PE/ DVT) found in other smaller studies. Similarly, these studies are more likely to focus on populations with higher COVID-19 severity, where our study captured all hospital admissions[41]. This protocol did not include a non-SARS-CoV-2 comparator group, which may provide useful data to compare complication burdens to other causes of critical illness or viral infection. Thirdly, owing to logistical constraints, we did not capture data on the timings of each complication. As our study was an urgent response to the emerging

pandemic, it would not have been possible to identify exactly when each complication started for such a large number of patients. Data around timings may in future help to identify sequences of events which lead to further deterioration. Fourthly, our data can only provide estimates of who gets complications in a hospitalised population. We found that even in previously healthy adults with no recorded comorbidity, complications affected more than 4 in 10 hospitalised patients; the effect and burden in the community remains undescribed. For infection related outcomes, we systematically classified microbiological culture results to identify whether infections were caused by pathogenic organisms. However, individuals may have acquired these in the community, so our estimates encompass both hospital and community acquired infection. In addition to this, the UK health service was under considerable pressure, which could have resulted in preferential admission to hospital of patients with the most severe disease. This may lead to an increase in the observed complication rate, as individuals with milder disease were managed at home. However, the risk of this is reduced by the multicentre design of our study, as peaks in hospital admissions varied in the UK over time. Compared to other international cohorts, our study had a higher observed hospital case fatality rate[42–45]. The reasons for this are multifactorial, and could relate to differences in testing strategy, thresholds for hospital admission, pre-existing population morbidity, and healthcare system preparedness. Finally, our data were collected from real-world observed clinical practice and patients did not undergo any additional tests to detect the presence of complications. Therefore, the true burden of complications is likely to be higher. However, performing large numbers of invasive tests may not be acceptable for patients, particularly in patients who are unlikely to survive or cannot tolerate investigations, and would be logistically challenging in study of this size.

Policy makers and healthcare planners should anticipate that large amounts of health and social care resource will be required to support those who survive COVID-19. This includes adequate provision of staffing and equipment; for example, provision of follow-up clinics for those who have sustained in-hospital complications such as acute kidney injury or respiratory tract infection. Beyond the short-term, further work is underway to establish the consequences of these complications and whether these are transient, or linked to worse long-term outcomes. Data on long-term health difficulties posed by COVID-19 will be of great importance, particularly as a large proportion of COVID-19 survivors come from economically active age groups. This should be considered on a policy level in terms of return to work and education; but importantly, it may have impacts on individual behaviour around perceived benefits of engaging with preventative measures including vaccination.

In summary, high rates of complications and poor functional outcomes were present in survivors of COVID-19, including in young and previously healthy individuals. Those over 50 years old and those admitted to critical care were at the highest risk. Common COVID-19 complications identified here are known to be associated with long-term morbidity and an increased risk of death.

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Author contributions

Conception of analysis, data analysis, data interpretation, writing and revision (TMD, AMR, EMH, ABD, MGS); Data analysis (CE, RP, LN); Study design and coordination (HEH, DP, KAH, LM, LS, MG, CJ, PO, GC); Data interpretation, writing and revision (CJF, SRK, CAS, KAM, AH, CDR, TS, LT, JVT, PJMO); Data interpretation, writing and critical review (AART, FS, OVS, MS, TdS, JD, JKB, MGS). All authors critical review and revision of draft manuscript. TMD, AMR, ABD, LN, RP and EMH all had access to the underlying data and verified the findings. TMD, EMH and MGS were responsible for manuscript submission. All authors have seen and approved the final text.

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Figures

Figure 1 – Patient inclusion flowchart

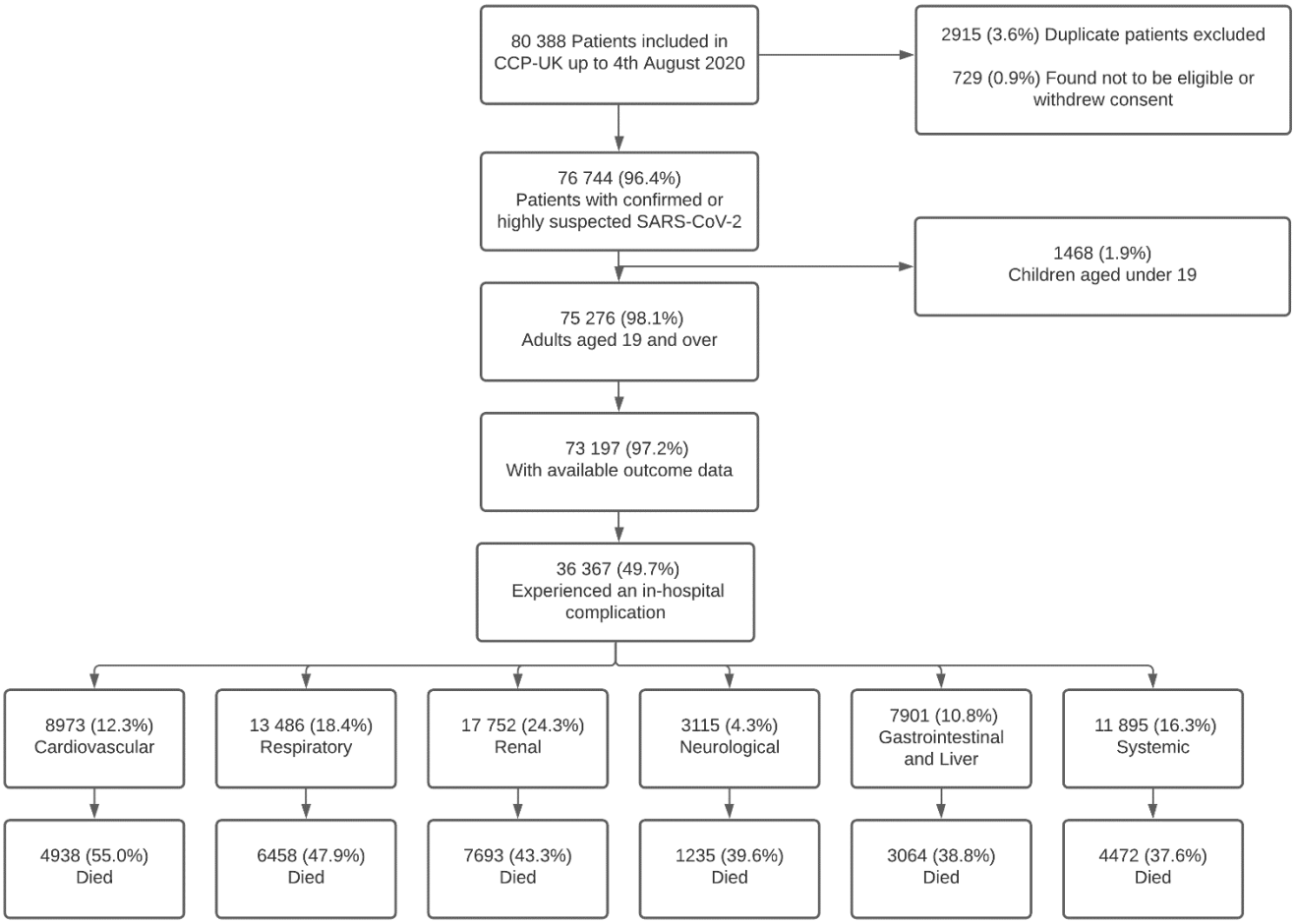


Figure 2 – Outcomes and mortality after complications. (A) Differences in complication rates, age, sex and comorbidity. (B) Kaplan-Meier survival curve stratified by number of complications experienced. (C) Hazard Ratios for effect of organ-specific complications on overall survival, adjusted for age, sex, deprivation and centre; supplement pp 14-20 for full models. Error bars represent 95% confidence intervals. (D) Effect of organ-specific complications on odds of being admitted to critical care; supplement pp 21-27 for full models. Error bars represent 95% confidence intervals.

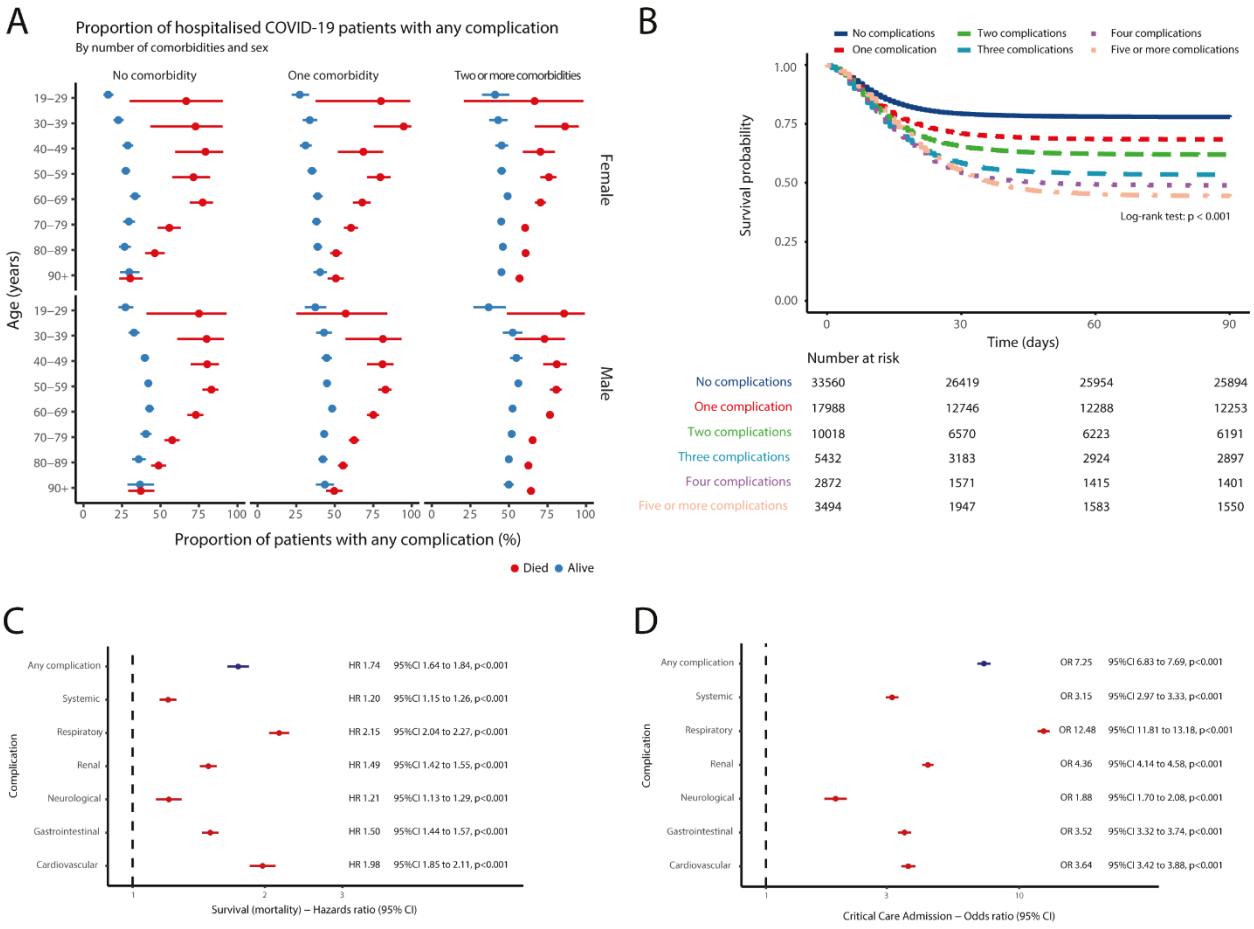


Figure 3 – Relationship between age, sex, comorbidities and adjusted outcomes using generalised additive models. (A) Shows relationships for the outcome of adjusted risk of any complication. (B) Shows relationships for the outcome of adjusted mortality risk, stratified by presence of complications. Each line represents one bootstrap replicate (i.e. one simulated patient). Supplement pp 39- 44 shows models for other organ-specific complications.

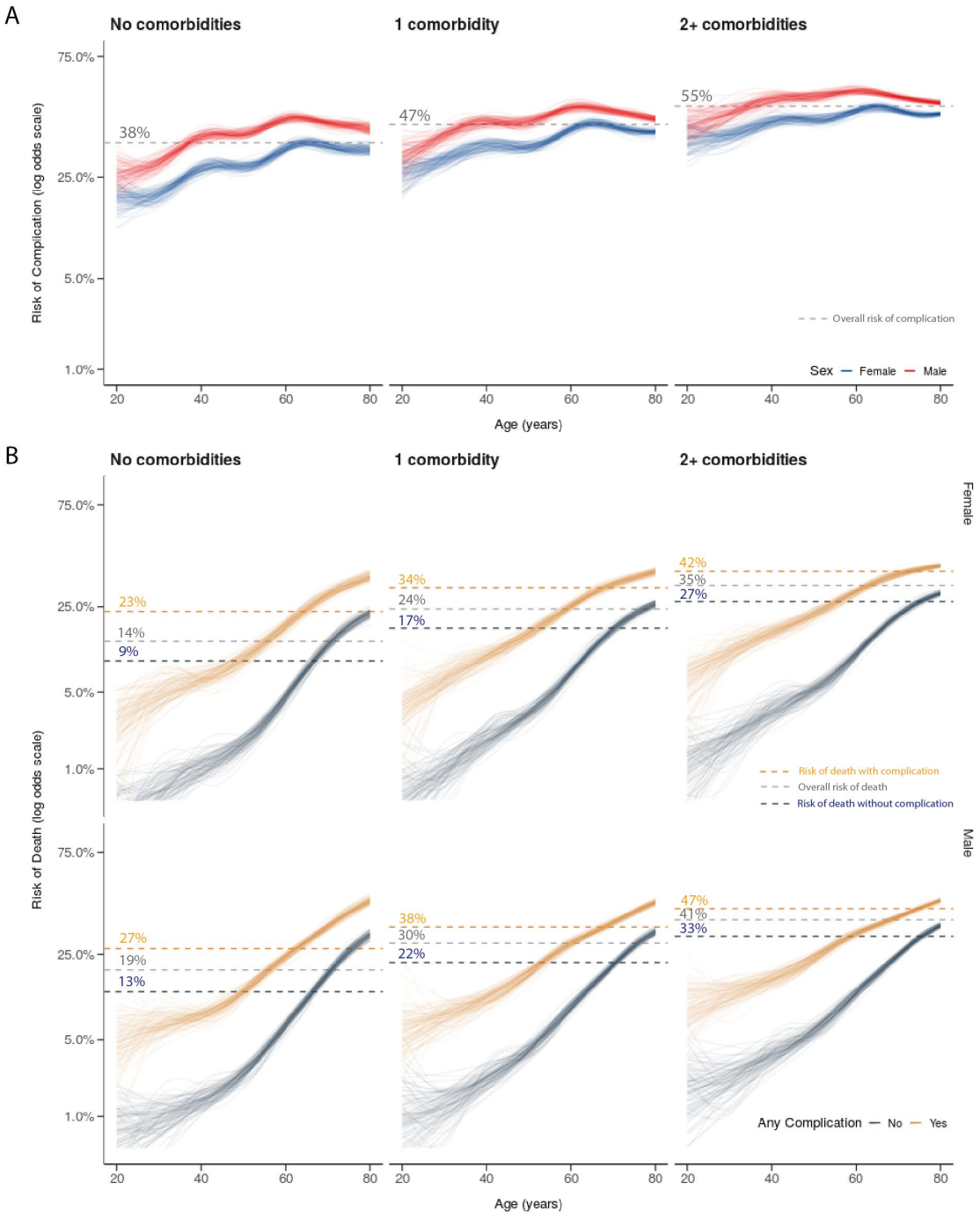
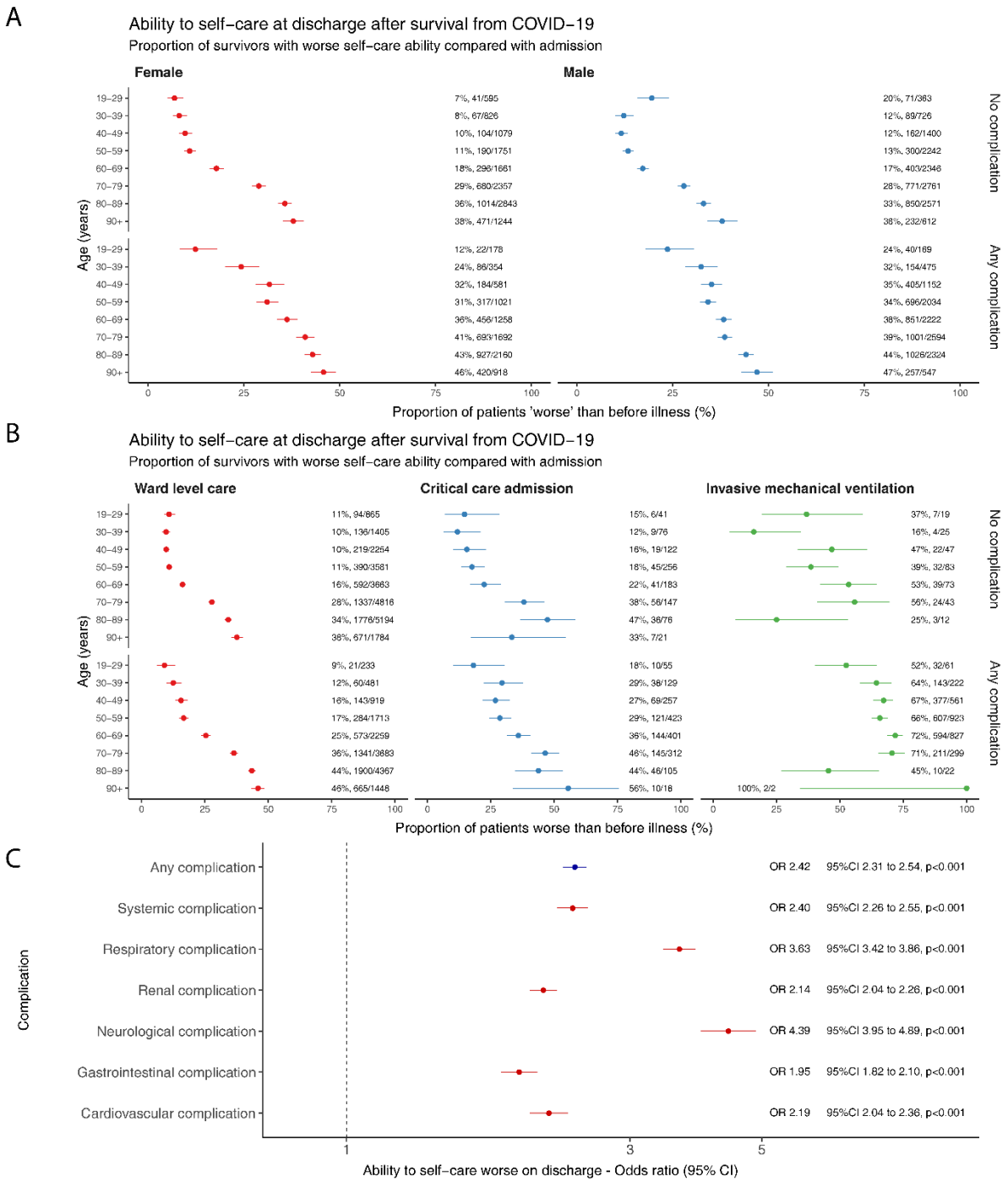


Figure 4 – (A) Ability to self-care at discharge in patients who experienced complications by age group and sex. Error bars represent 95% confidence intervals. (B) Ability to self-care at discharge by disease severity. Error bars represent 95% confidence intervals. (C) Adjusted odds of worse ability to self-care at discharge by organ-specific complications by complication in adults admitted to hospital with severe COVID-19; Supplementary table 11 – pp27-34 for full models. Error bars represent 95% confidence intervals.



Tables

Table 1 – Patient characteristics by organ-specific complications experienced.

		Patients experiencing complications		Organ-specific level complications					
		Total patients	Any complication	Systemic	Renal	GI	Cardiovascular	Neurological	Respiratory*
Total N (%)		73197	36367 (49.7)	11895 (16.3)	17752 (24.3)	7901 (10.8)	8973 (12.3)	3115 (4.3)	13486 (18.4)
Age on admission	18-29	1500 (2.0)	411 (1.1)	147 (1.2)	126 (0.7)	139 (1.8)	47 (0.5)	38 (1.2)	145 (1.1)
	30-39	2753 (3.8)	1015 (2.8)	376 (3.2)	353 (2.0)	365 (4.6)	134 (1.5)	91 (2.9)	457 (3.4)
	40-49	4996 (6.8)	2170 (6.0)	731 (6.1)	874 (4.9)	740 (9.4)	370 (4.1)	162 (5.2)	1169 (8.7)
	50-59	9101 (12.4)	4418 (12.1)	1504 (12.6)	2078 (11.7)	1468 (18.6)	847 (9.4)	352 (11.3)	2263 (16.8)
	60-69	11139 (15.2)	5954 (16.4)	2008 (16.9)	3055 (17.2)	1578 (20.0)	1389 (15.5)	500 (16.1)	2767 (20.5)
	70-79	16563 (22.6)	8549 (23.5)	2727 (22.9)	4318 (24.3)	1644 (20.8)	2220 (24.7)	725 (23.3)	2978 (22.1)
	80-89	19900 (27.2)	10207 (28.1)	3241 (27.2)	5161 (29.1)	1478 (18.7)	2888 (32.2)	941 (30.2)	2761 (20.5)
	90+	7245 (9.9)	3643 (10.0)	1161 (9.8)	1787 (10.1)	489 (6.2)	1078 (12.0)	306 (9.8)	946 (7.0)
Sex at Birth	Female	31977 (43.7)	14521 (39.9)	4872 (41.0)	6612 (37.2)	2690 (34.0)	3539 (39.4)	1289 (41.4)	4951 (36.7)
	Male	41025 (56.0)	21758 (59.8)	7001 (58.9)	11097 (62.5)	5199 (65.8)	5415 (60.3)	1822 (58.5)	8504 (63.1)
	(Missing)	195 (0.3)	88 (0.2)	22 (0.2)	43 (0.2)	12 (0.2)	19 (0.2)	4 (0.1)	31 (0.2)
Deprivation	1	10408 (14.2)	5201 (14.3)	1773 (14.9)	2437 (13.7)	1152 (14.6)	1384 (15.4)	466 (15.0)	1885 (14.0)
	2	12853 (17.6)	6439 (17.7)	2147 (18.0)	2996 (16.9)	1431 (18.1)	1634 (18.2)	552 (17.7)	2305 (17.1)
	3	15822 (21.6)	7855 (21.6)	2595 (21.8)	3793 (21.4)	1631 (20.6)	1986 (22.1)	633 (20.3)	3035 (22.5)
	4	16104 (22.0)	8069 (22.2)	2621 (22.0)	4101 (23.1)	1748 (22.1)	2012 (22.4)	718 (23.0)	3083 (22.9)
	5	17997 (24.6)	8801 (24.2)	2759 (23.2)	4424 (24.9)	1939 (24.5)	1956 (21.8)	745 (23.9)	3177 (23.6)
	(Missing)	13 (0.0)	2 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)	1 (0.0)	1 (0.0)	1 (0.0)
Ethnicity	White	53780 (73.5)	26431 (72.7)	8678 (73.0)	12896 (72.6)	5438 (68.8)	6624 (73.8)	2282 (73.3)	9173 (68.0)
	South Asian	3318 (4.5)	1630 (4.5)	593 (5.0)	799 (4.5)	441 (5.6)	369 (4.1)	102 (3.3)	777 (5.8)
	East Asian	484 (0.7)	249 (0.7)	96 (0.8)	113 (0.6)	82 (1.0)	55 (0.6)	15 (0.5)	142 (1.1)
	Black	2480 (3.4)	1433 (3.9)	508 (4.3)	822 (4.6)	346 (4.4)	306 (3.4)	114 (3.7)	627 (4.6)
	Other Ethnic Minority	4646 (6.3)	2435 (6.7)	751 (6.3)	1145 (6.4)	641 (8.1)	491 (5.5)	203 (6.5)	1171 (8.7)
	(Missing)	8489 (11.6)	4189 (11.5)	1269 (10.7)	1977 (11.1)	953 (12.1)	1128 (12.6)	399 (12.8)	1596 (11.8)
Diabetes	No	49765 (75.8)	24481 (73.6)	7878 (71.9)	11265 (69.7)	5694 (77.9)	5948 (72.4)	2173 (77.7)	9194 (74.3)
	Yes	15855 (24.2)	8792 (26.4)	3081 (28.1)	4891 (30.3)	1615 (22.1)	2266 (27.6)	625 (22.3)	3173 (25.7)
Obesity	No	53415 (73.0)	26397 (72.6)	8476 (71.3)	12656 (71.3)	5784 (73.2)	6331 (70.6)	2304 (74.0)	9498 (70.4)
	Yes	7329 (10.0)	4230 (11.6)	1583 (13.3)	2208 (12.4)	985 (12.5)	1226 (13.7)	296 (9.5)	2059 (15.3)
	(Missing)	12453 (17.0)	5740 (15.8)	1836 (15.4)	2888 (16.3)	1132 (14.3)	1416 (15.8)	515 (16.5)	1929 (14.3)
Chronic Cardiac Disease	No	45563 (62.2)	21808 (60.0)	7117 (59.8)	10400 (58.6)	5332 (67.5)	4077 (45.4)	1923 (61.7)	8787 (65.2)
	Yes	22563 (30.8)	12758 (35.1)	4235 (35.6)	6436 (36.3)	2201 (27.9)	4496 (50.1)	995 (31.9)	4025 (29.8)
	(Missing)	5071 (6.9)	1801 (5.0)	543 (4.6)	916 (5.2)	368 (4.7)	400 (4.5)	197 (6.3)	674 (5.0)
Chronic pulmonary disease	No	55604 (76.0)	27916 (76.8)	9261 (77.9)	13619 (76.7)	6404 (81.1)	6665 (74.3)	2461 (79.0)	10468 (77.6)
	Yes	12235 (16.7)	6472 (17.8)	2002 (16.8)	3143 (17.7)	1100 (13.9)	1791 (20.0)	444 (14.3)	2289 (17.0)
	(Missing)	5358 (7.3)	1979 (5.4)	632 (5.3)	990 (5.6)	397 (5.0)	517 (5.8)	210 (6.7)	729 (5.4)
Asthma	No	58352 (79.7)	29806 (82.0)	9782 (82.2)	14657 (82.6)	6525 (82.6)	7286 (81.2)	2572 (82.6)	10852 (80.5)
	Yes	9298 (12.7)	4447 (12.2)	1482 (12.5)	2039 (11.5)	977 (12.4)	1141 (12.7)	320 (10.3)	1849 (13.7)
	(Missing)	5547 (7.6)	2114 (5.8)	631 (5.3)	1056 (5.9)	399 (5.0)	546 (6.1)	223 (7.2)	785 (5.8)
Chronic kidney disease	No	55458 (75.8)	26793 (73.7)	8582 (72.1)	11962 (67.4)	6284 (79.5)	6434 (71.7)	2368 (76.0)	10654 (79.0)
	Yes	12182 (16.6)	7503 (20.6)	2661 (22.4)	4785 (27.0)	1166 (14.8)	2008 (22.4)	525 (16.9)	2070 (15.3)
	(Missing)	5557 (7.6)	2071 (5.7)	652 (5.5)	1005 (5.7)	451 (5.7)	531 (5.9)	222 (7.1)	762 (5.7)
Moderate or severe liver disease	No	65646 (89.7)	33005 (90.8)	10769 (90.5)	16111 (90.8)	6879 (87.1)	8162 (91.0)	2764 (88.7)	12314 (91.3)
	Yes	1340 (1.8)	916 (2.5)	358 (3.0)	413 (2.3)	528 (6.7)	179 (2.0)	96 (3.1)	281 (2.1)
	(Missing)	6211 (8.5)	2446 (6.7)	768 (6.5)	1228 (6.9)	494 (6.3)	632 (7.0)	255 (8.2)	891 (6.6)
Mild Liver disease	No	65784 (89.9)	33164 (91.2)	10837 (91.1)	16169 (91.1)	7096 (89.8)	8178 (91.1)	2792 (89.6)	12338 (91.5)
	Yes	1035 (1.4)	635 (1.7)	240 (2.0)	294 (1.7)	269 (3.4)	132 (1.5)	60 (1.9)	222 (1.6)
	(Missing)	6378 (8.7)	2568 (7.1)	818 (6.9)	1289 (7.3)	536 (6.8)	663 (7.4)	263 (8.4)	926 (6.9)
Chronic neurological disorder	No	58511 (79.9)	29546 (81.2)	9725 (81.8)	14440 (81.3)	6700 (84.8)	7357 (82.0)	2048 (65.7)	11352 (84.2)
	Yes	8802 (12.0)	4559 (12.5)	1467 (12.3)	2167 (12.2)	729 (9.2)	1024 (11.4)	845 (27.1)	1309 (9.7)
	(Missing)	5884 (8.0)	2262 (6.2)	703 (5.9)	1145 (6.4)	472 (6.0)	592 (6.6)	222 (7.1)	825 (6.1)
Malignant neoplasm	No	60050 (82.0)	29952 (82.4)	9485 (79.7)	14643 (82.5)	6620 (83.8)	7378 (82.2)	2564 (82.3)	11283 (83.7)
	Yes	7072 (9.7)	4075 (11.2)	1675 (14.1)	1932 (10.9)	819 (10.4)	994 (11.1)	307 (9.9)	1341 (9.9)
	(Missing)	6075 (8.3)	2340 (6.4)	735 (6.2)	1177 (6.6)	462 (5.8)	601 (6.7)	244 (7.8)	862 (6.4)
Chronic hematologic disease	No	64082 (87.5)	32079 (88.2)	10150 (85.3)	15622 (88.0)	6958 (88.1)	7906 (88.1)	2737 (87.9)	12003 (89.0)
	Yes	2982 (4.1)	1907 (5.2)	1017 (8.5)	942 (5.3)	447 (5.7)	461 (5.1)	122 (3.9)	600 (4.4)
	(Missing)	6133 (8.4)	2381 (6.5)	728 (6.1)	1188 (6.7)	496 (6.3)	606 (6.8)	256 (8.2)	883 (6.5)
HIV/AIDs	No	65920 (90.1)	33268 (91.5)	10828 (91.0)	16190 (91.2)	7256 (91.8)	8195 (91.3)	2809 (90.2)	12360 (91.7)
	Yes	256 (0.3)	149 (0.4)	57 (0.5)	82 (0.5)	42 (0.5)	28 (0.3)	13 (0.4)	57 (0.4)
	(Missing)	7021 (9.6)	2950 (8.1)	1010 (8.5)	1480 (8.3)	603 (7.6)	750 (8.4)	293 (9.4)	1069 (7.9)

Rheumatologic disorder	No	59168 (80.8)	29823 (82.0)	9663 (81.2)	14540 (81.9)	6708 (84.9)	7294 (81.3)	2512 (80.6)	11245 (83.4)
	Yes	7724 (10.6)	4075 (11.2)	1462 (12.3)	1961 (11.0)	701 (8.9)	1061 (11.8)	353 (11.3)	1358 (10.1)
	(Missing)	6305 (8.6)	2469 (6.8)	770 (6.5)	1251 (7.0)	492 (6.2)	618 (6.9)	250 (8.0)	883 (6.5)
Dementia	No	55758 (76.2)	28473 (78.3)	9548 (80.3)	13583 (76.5)	6708 (84.9)	7079 (78.9)	2237 (71.8)	11449 (84.9)
	Yes	11682 (16.0)	5668 (15.6)	1624 (13.7)	3064 (17.3)	750 (9.5)	1306 (14.6)	645 (20.7)	1239 (9.2)
	(Missing)	5757 (7.9)	2226 (6.1)	723 (6.1)	1105 (6.2)	443 (5.6)	588 (6.6)	233 (7.5)	798 (5.9)
Smoking	Never Smoked	23944 (32.7)	11976 (32.9)	4071 (34.2)	5577 (31.4)	2811 (35.6)	2872 (32.0)	889 (28.5)	4894 (36.3)
	Current Smoker	3895 (5.3)	1927 (5.3)	677 (5.7)	875 (4.9)	508 (6.4)	459 (5.1)	188 (6.0)	694 (5.1)
	Former Smoker	15834 (21.6)	8533 (23.5)	2914 (24.5)	4179 (23.5)	1740 (22.0)	2317 (25.8)	630 (20.2)	3304 (24.5)
	(Missing)	29524 (40.3)	13931 (38.3)	4233 (35.6)	7121 (40.1)	2842 (36.0)	3325 (37.1)	1408 (45.2)	4594 (34.1)

Percentage values are column percentages. * = Severe acute respiratory infection was contained within case definition so was not counted as a complication. HIV/AIDS - Human immunodeficiency virus infection and acquired immunodeficiency syndrome, IMD – Index of Multiple Deprivation. GI – Gastrointestinal (including liver).

Table 2 - Outcomes by organ specific complications.

		Patients experiencing complications		Organ-specific level complications					
		Total patients	Any complication	Systemic	Renal	GI	Cardiovascular	Neurological	Respiratory*
Total N (%)		73197	36367 (49.7)	11895 (16.3)	17752 (24.3)	7901 (10.8)	8973 (12.3)	3115 (4.3)	13486 (18.4)
Death	No	50105 (68.5)	21784 (59.9)	7423 (62.4)	10059 (56.7)	4837 (61.2)	4035 (45.0)	1880 (60.4)	7028 (52.1)
	Yes	23092 (31.5)	14583 (40.1)	4472 (37.6)	7693 (43.3)	3064 (38.8)	4938 (55.0)	1235 (39.6)	6458 (47.9)
Critical Care Admission	No	62125 (84.9)	28092 (77.2)	8804 (74.0)	12992 (73.2)	5139 (65.0)	6640 (74.0)	2446 (78.5)	7472 (55.4)
	Yes	10034 (13.7)	8267 (22.7)	3090 (26.0)	4755 (26.8)	2760 (34.9)	2333 (26.0)	668 (21.4)	6012 (44.6)
	(Missing)	1038 (1.4)	8 (0.0)	1 (0.0)	5 (0.0)	2 (0.0)	0 (0.0)	1 (0.0)	2 (0.0)
Any invasive ventilation	No	65888 (90.0)	30710 (84.4)	9556 (80.3)	14262 (80.3)	5815 (73.6)	7186 (80.1)	2573 (82.6)	8809 (65.3)
	Yes	6122 (8.4)	5619 (15.5)	2330 (19.6)	3471 (19.6)	2077 (26.3)	1784 (19.9)	542 (17.4)	4670 (34.6)
	(Missing)	1187 (1.6)	38 (0.1)	9 (0.1)	19 (0.1)	9 (0.1)	3 (0.0)	0 (0.0)	7 (0.1)
Any non-invasive ventilation	No	60035 (84.7)	28202 (78.5)	9228 (78.2)	13361 (76.1)	5685 (72.8)	6862 (77.1)	2566 (83.3)	8332 (62.3)
	Yes	10827 (15.3)	7741 (21.5)	2567 (21.8)	4194 (23.9)	2124 (27.2)	2034 (22.9)	513 (16.7)	5038 (37.7)
Any oxygen	No	17652 (24.7)	5971 (16.5)	2079 (17.6)	2470 (14.0)	1153 (14.7)	1190 (13.3)	737 (23.8)	838 (6.2)
	Yes	53695 (75.3)	30181 (83.5)	9762 (82.4)	15189 (86.0)	6705 (85.3)	7744 (86.7)	2358 (76.2)	12598 (93.8)

Percentage values are row percentages, except for totals which represent column percentages. * = Severe acute respiratory infection was contained within case definition so was not counted as a complication. GI – Gastrointestinal (including liver).

Online supplement

Supplementary table 1 – Definition of in-hospital complications

Organ specific complication	Complication within this group	Definition
Respiratory	Bacterial pneumonia (highly likely)	Clinically significant organism detected in sputum or deep respiratory culture
	Bacterial pneumonia (suspected)	Defined clinically in patient healthcare record
	Likely Acute Respiratory Distress Syndrome (ARDS)	Defined clinically in patient record or defined as one of the following combinations: - receiving extracorporeal membrane oxygenation - being nursed in a prone position and receiving invasive mechanical ventilation - receiving mechanical ventilation and having a PF (*PaO2/FiO2*) ratio of 300 or less
	Empyema	Defined clinically in patient healthcare record
	Pneumothorax	Defined clinically in patient healthcare record
	Pleural effusion	Defined clinically in patient healthcare record
Neurological	Meningitis	Defined clinically in patient healthcare record
	Encephalitis	Defined clinically in patient healthcare record
	Seizure	Defined clinically in patient healthcare record
	Stroke	Defined clinically in patient healthcare record
Cardiovascular	Thromboembolism	Defined clinically in patient healthcare record
	Heart Failure	Defined clinically in patient healthcare record
	Myocarditis	Defined clinically in patient healthcare record
	Endocarditis	Defined clinically in patient healthcare record
	Arrhythmia	Defined clinically in patient healthcare record
	Cardiomyopathy	Defined clinically in patient healthcare record
	Myocardial Ischaemia	Defined clinically in patient healthcare record
	Cardiac Arrest	Defined clinically in patient healthcare record
Renal	Acute Kidney Injury	Creatinine rise which corresponded to Kidney Disease Improving Global Outcomes (KDIGO) stage I or above (creatinine rise ≥1.5x baseline value or by ≥26.5 μmol/L) Urine output not included within this definition
Gastrointestinal	Acute Liver Injury	Any of the following: - International normalised ratio (INR) rise of 2.5 times or greater than the lowest entered value - INR of over 4.5 (in the absence of warfarin therapy)

		- Alanine aminotransferase (ALT) rise of greater than 10 times the lowest value - ALT over 150 - Bilirubin rise of greater than 15 - Bilirubin greater than 55 (in the absence of any pre-existing liver disease)
	Pancreatitis	Defined clinically in patient healthcare record
	Gastrointestinal haemorrhage	Defined clinically in patient healthcare record
Systemic	Coagulopathy	Defined clinically in patient healthcare record
	Disseminated Intravascular Coagulation	Defined clinically in patient healthcare record
	Anaemia	Defined clinically in patient healthcare record
	Bloodstream Infection	Clinically significant sample in blood culture

3

Supplementary table 2 – Complication rates by SARS-CoV-2 RT-PCR positivity status

		Total	Any complication	Systemic	Renal	Gastrointestinal	Cardiovascular	Neurological	Respiratory
Total N (%)		73197	36367 (49.7)	11895 (16.3)	17752 (24.3)	7901 (10.8)	8973 (12.3)	3115 (4.3)	13486 (18.4)
PCR	Confirmed	62894 (85.9)	32044 (50.9)	10617 (16.9)	15829 (25.2)	6916 (11.0)	7935 (12.6)	2753 (4.4)	11849 (18.8)
	Not confirmed	10303 (14.1)	4323 (42.0)	1278 (12.4)	1923 (18.7)	985 (9.6)	1038 (10.1)	362 (3.5)	1637 (15.9)

Percentage values are row percentages, except for totals which represent column percentages.

Supplementary table 3A - Specific complications stratified by age and sex in adults admitted to hospital with severe COVID-19.

			Age (years)							
		Total	19-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
Female	Total N (%)	31977	882 (2.8)	1359 (4.2)	1960 (6.1)	3488 (10.9)	4231 (13.2)	6685 (20.9)	9178 (28.7)	4194 (13.1)
	Cryptogenic organizing pneumonia	42 (0.1)	0 (0.0)	2 (0.1)	2 (0.1)	4 (0.1)	8 (0.2)	6 (0.1)	10 (0.1)	10 (0.2)
	Likely ARDS	3251 (10.2)	53 (6.0)	145 (10.7)	313 (16.0)	550 (15.8)	703 (16.6)	662 (9.9)	602 (6.6)	223 (5.3)
	Pneumothorax	227 (0.7)	6 (0.7)	11 (0.8)	25 (1.3)	39 (1.1)	57 (1.3)	52 (0.8)	28 (0.3)	9 (0.2)
	Pleural effusion	1940 (6.1)	16 (1.8)	47 (3.5)	84 (4.3)	143 (4.1)	269 (6.4)	421 (6.3)	641 (7.0)	319 (7.6)
	Highly likely Bacterial Pneumonia	99 (0.3)	2 (0.2)	4 (0.3)	14 (0.7)	25 (0.7)	21 (0.5)	21 (0.3)	10 (0.1)	2 (0.0)
	Meningitis / Encephalitis	61 (0.2)	2 (0.2)	4 (0.3)	7 (0.4)	7 (0.2)	19 (0.4)	8 (0.1)	11 (0.1)	3 (0.1)
	Seizure	331 (1.0)	6 (0.7)	17 (1.3)	22 (1.1)	46 (1.3)	46 (1.1)	79 (1.2)	87 (0.9)	28 (0.7)
	Stroke / Cerebrovascular accident	483 (1.5)	2 (0.2)	5 (0.4)	14 (0.7)	32 (0.9)	67 (1.6)	106 (1.6)	175 (1.9)	82 (2.0)
	Other neurological complication	537 (1.7)	7 (0.8)	8 (0.6)	22 (1.1)	42 (1.2)	69 (1.6)	105 (1.6)	201 (2.2)	83 (2.0)
	Congestive heart failure	1133 (3.5)	0 (0.0)	5 (0.4)	16 (0.8)	34 (1.0)	93 (2.2)	243 (3.6)	486 (5.3)	256 (6.1)
	Endocarditis / Myocarditis Pericarditis	83 (0.3)	1 (0.1)	5 (0.4)	6 (0.3)	11 (0.3)	19 (0.4)	23 (0.3)	14 (0.2)	4 (0.1)
	Myocarditis / Pericarditis	70 (0.2)	3 (0.3)	4 (0.3)	5 (0.3)	13 (0.4)	16 (0.4)	13 (0.2)	10 (0.1)	6 (0.1)
	Cardiomyopathy	79 (0.2)	0 (0.0)	1 (0.1)	6 (0.3)	10 (0.3)	8 (0.2)	16 (0.2)	29 (0.3)	9 (0.2)
	Cardiac arrhythmia	1907 (6.0)	15 (1.7)	30 (2.2)	87 (4.4)	140 (4.0)	226 (5.3)	429 (6.4)	680 (7.4)	300 (7.2)
	Cardiac ischemia	381 (1.2)	0 (0.0)	3 (0.2)	6 (0.3)	29 (0.8)	42 (1.0)	90 (1.3)	138 (1.5)	73 (1.7)
	Cardiac arrest	653 (2.0)	5 (0.6)	13 (1.0)	25 (1.3)	65 (1.9)	93 (2.2)	161 (2.4)	200 (2.2)	91 (2.2)
	Bloodstream infection	404 (1.3)	6 (0.7)	22 (1.6)	34 (1.7)	48 (1.4)	71 (1.7)	76 (1.1)	105 (1.1)	42 (1.0)
	Coagulation disorder / DIC	724 (2.3)	14 (1.6)	24 (1.8)	46 (2.3)	101 (2.9)	135 (3.2)	146 (2.2)	190 (2.1)	68 (1.6)
	Anaemia	4126 (12.9)	81 (9.2)	160 (11.8)	250 (12.8)	432 (12.4)	628 (14.8)	856 (12.8)	1188 (12.9)	531 (12.7)
	Rhabdomyolysis / Myositis	99 (0.3)	3 (0.3)	1 (0.1)	1 (0.1)	9 (0.3)	11 (0.3)	15 (0.2)	36 (0.4)	23 (0.5)
	Acute Kidney Injury	6612 (20.7)	51 (5.8)	124 (9.1)	251 (12.8)	642 (18.4)	933 (22.1)	1533 (22.9)	2137 (23.3)	941 (22.4)
	Gastrointestinal haemorrhage	325 (1.0)	5 (0.6)	8 (0.6)	8 (0.4)	25 (0.7)	48 (1.1)	57 (0.9)	120 (1.3)	54 (1.3)
	Pancreatitis	108 (0.3)	5 (0.6)	9 (0.7)	9 (0.5)	17 (0.5)	24 (0.6)	16 (0.2)	22 (0.2)	6 (0.1)
	Deep Vein Thrombosis	167 (0.5)	2 (0.2)	10 (0.7)	9 (0.5)	31 (0.9)	33 (0.8)	30 (0.4)	41 (0.4)	11 (0.3)
	Pulmonary Embolism	382 (1.2)	3 (0.3)	15 (1.1)	27 (1.4)	65 (1.9)	83 (2.0)	78 (1.2)	90 (1.0)	21 (0.5)
	Liver Injury	2366 (7.4)	48 (5.4)	113 (8.3)	192 (9.8)	409 (11.7)	430 (10.2)	475 (7.1)	500 (5.4)	199 (4.7)
Male	Total N (%)	41025	612 (1.5)	1385 (3.4)	3021 (7.4)	5591 (13.6)	6882 (16.8)	9841 (24.0)	10662 (26.0)	3031 (7.4)
	Cryptogenic organizing pneumonia	50 (0.1)	0 (0.0)	2 (0.1)	4 (0.1)	9 (0.2)	12 (0.2)	10 (0.1)	12 (0.1)	1 (0.0)
	Likely ARDS	6417 (15.6)	62 (10.1)	247 (17.8)	697 (23.1)	1376 (24.6)	1540 (22.4)	1411 (14.3)	889 (8.3)	195 (6.4)
	Pneumothorax	466 (1.1)	6 (1.0)	20 (1.4)	47 (1.6)	113 (2.0)	121 (1.8)	87 (0.9)	55 (0.5)	17 (0.6)
	Pleural effusion	2583 (6.3)	23 (3.8)	53 (3.8)	145 (4.8)	322 (5.8)	452 (6.6)	631 (6.4)	723 (6.8)	234 (7.7)
	Highly likely Bacterial Pneumonia	260 (0.6)	1 (0.2)	10 (0.7)	38 (1.3)	78 (1.4)	60 (0.9)	54 (0.5)	17 (0.2)	2 (0.1)
	Meningitis / Encephalitis	95 (0.2)	5 (0.8)	5 (0.4)	14 (0.5)	20 (0.4)	23 (0.3)	12 (0.1)	16 (0.2)	0 (0.0)
	Seizure	497 (1.2)	13 (2.1)	33 (2.4)	45 (1.5)	89 (1.6)	87 (1.3)	105 (1.1)	105 (1.0)	20 (0.7)
	Stroke / Cerebrovascular accident	729 (1.8)	1 (0.2)	12 (0.9)	36 (1.2)	75 (1.3)	147 (2.1)	205 (2.1)	209 (2.0)	44 (1.5)
	Other neurological complication	696 (1.7)	7 (1.1)	18 (1.3)	31 (1.0)	90 (1.6)	98 (1.4)	175 (1.8)	211 (2.0)	66 (2.2)

		Age (years)							
	Total	19-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
Congestive heart failure	1387 (3.4)	0 (0.0)	11 (0.8)	27 (0.9)	84 (1.5)	184 (2.7)	363 (3.7)	539 (5.1)	179 (5.9)
Endocarditis / Myocarditis Pericarditis	181 (0.4)	1 (0.2)	12 (0.9)	19 (0.6)	29 (0.5)	44 (0.6)	39 (0.4)	36 (0.3)	1 (0.0)
Myocarditis / Pericarditis	121 (0.3)	1 (0.2)	3 (0.2)	20 (0.7)	19 (0.3)	22 (0.3)	28 (0.3)	22 (0.2)	6 (0.2)
Cardiomyopathy	94 (0.2)	0 (0.0)	3 (0.2)	9 (0.3)	13 (0.2)	20 (0.3)	24 (0.2)	21 (0.2)	4 (0.1)
Cardiac arrhythmia	2933 (7.1)	20 (3.3)	48 (3.5)	143 (4.7)	367 (6.6)	597 (8.7)	790 (8.0)	759 (7.1)	209 (6.9)
Cardiac ischemia	615 (1.5)	0 (0.0)	11 (0.8)	19 (0.6)	56 (1.0)	106 (1.5)	175 (1.8)	186 (1.7)	62 (2.0)
Cardiac arrest	1249 (3.0)	4 (0.7)	19 (1.4)	68 (2.3)	175 (3.1)	238 (3.5)	327 (3.3)	315 (3.0)	103 (3.4)
Bloodstream infection	710 (1.7)	9 (1.5)	29 (2.1)	65 (2.2)	99 (1.8)	142 (2.1)	154 (1.6)	166 (1.6)	46 (1.5)
Coagulation disorder / DIC	1343 (3.3)	13 (2.1)	56 (4.0)	131 (4.3)	258 (4.6)	272 (4.0)	292 (3.0)	253 (2.4)	68 (2.2)
Anaemia	5762 (14.0)	39 (6.4)	143 (10.3)	327 (10.8)	791 (14.1)	1043 (15.2)	1432 (14.6)	1534 (14.4)	453 (14.9)
Rhabdomyolysis / Myositis	165 (0.4)	5 (0.8)	6 (0.4)	12 (0.4)	24 (0.4)	18 (0.3)	42 (0.4)	41 (0.4)	17 (0.6)
Acute Kidney Injury	11097 (27.0)	75 (12.3)	228 (16.5)	620 (20.5)	1434 (25.6)	2116 (30.7)	2775 (28.2)	3007 (28.2)	842 (27.8)
Gastrointestinal haemorrhage	529 (1.3)	5 (0.8)	9 (0.6)	32 (1.1)	65 (1.2)	91 (1.3)	120 (1.2)	159 (1.5)	48 (1.6)
Pancreatitis	139 (0.3)	6 (1.0)	18 (1.3)	18 (0.6)	36 (0.6)	21 (0.3)	23 (0.2)	14 (0.1)	3 (0.1)
Deep Vein Thrombosis	261 (0.6)	1 (0.2)	7 (0.5)	25 (0.8)	59 (1.1)	55 (0.8)	57 (0.6)	44 (0.4)	13 (0.4)
Pulmonary Embolism	622 (1.5)	11 (1.8)	14 (1.0)	78 (2.6)	139 (2.5)	136 (2.0)	135 (1.4)	96 (0.9)	13 (0.4)
Liver Injury	4732 (11.5)	80 (13.1)	223 (16.1)	515 (17.0)	988 (17.7)	1027 (14.9)	998 (10.1)	714 (6.7)	187 (6.2)

Percentage values are row percentages, except for totals which represent column percentages. ARDS – Acute Respiratory Distress Syndrome, DIC – Disseminated Intravascular Coagulation.

Supplementary table 3B – Comparison between suspected and highly likely bacterial pneumonia by age and sex in adults admitted to hospital with severe COVID-19.

			Age group (years)							
		Total N	19-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
Female	Total N (%)	31977	882 (2.8)	1359 (4.2)	1960 (6.1)	3488 (10.9)	4231 (13.2)	6685 (20.9)	9178 (28.7)	4194 (13.1)
	Suspected Bacterial Pneumonia	3533 (100)	43 (1.2)	101 (2.9)	188 (5.3)	403 (11.4)	539 (15.3)	771 (21.8)	1028 (29.1)	460 (13.0)
	Highly likely Bacterial Pneumonia	99 (100)	2 (2.0)	4 (4.0)	14 (14.1)	25 (25.3)	21 (21.2)	21 (21.2)	10 (10.1)	2 (2.0)
Male	Total N (%)	41025	612 (1.5)	1385 (3.4)	3021 (7.4)	5591 (13.6)	6882 (16.8)	9841 (24.0)	10662 (26.0)	3031 (7.4)
	Suspected Bacterial Pneumonia	5321 (100)	52 (1.0)	148 (2.8)	407 (7.6)	765 (14.4)	927 (17.4)	1281 (24.1)	1353 (25.4)	388 (7.3)
	Highly likely Bacterial Pneumonia	260 (100)	1 (0.4)	10 (3.8)	38 (14.6)	78 (30.0)	60 (23.1)	54 (20.8)	17 (6.5)	2 (0.8)

Percentage values are row percentages

Supplementary table 3C- Comparison between suspected and highly likely bacterial pneumonia by number of existing comorbidities in adults admitted to hospital with severe COVID-19.

Number of existing comorbidities on admission		Total N	Age group (years) 19-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
0	Total N (%)	13908	862 (6.2)	1430 (10.3)	2140 (15.4)	2907 (20.9)	2341 (16.8)	1925 (13.8)	1700 (12.2)	603 (4.3)
	Suspected Bacterial Pneumonia	1478	44 (3.0)	112 (7.6)	239 (16.2)	356 (24.1)	312 (21.1)	211 (14.3)	154 (10.4)	50 (3.4)
	Highly likely Bacterial Pneumonia	111	1 (0.9)	6 (5.4)	23 (20.7)	39 (35.1)	21 (18.9)	19 (17.1)	2 (1.8)	0 (0.0)
1	Total N (%)	17635	434 (2.5)	780 (4.4)	1550 (8.8)	2850 (16.2)	3031 (17.2)	3786 (21.5)	3768 (21.4)	1436 (8.1)
	Suspected Bacterial Pneumonia	2105	33 (1.6)	76 (3.6)	199 (9.5)	369 (17.5)	390 (18.5)	458 (21.8)	425 (20.2)	155 (7.4)
	Highly likely Bacterial Pneumonia	107	1 (0.9)	5 (4.7)	14 (13.1)	40 (37.4)	23 (21.5)	19 (17.8)	4 (3.7)	1 (0.9)
2+	Total N (%)	41654	204 (0.5)	543 (1.3)	1306 (3.1)	3344 (8.0)	5767 (13.8)	10852 (26.1)	14432 (34.6)	5206 (12.5)
	Suspected Bacterial Pneumonia	5288	18 (0.3)	62 (1.2)	160 (3.0)	445 (8.4)	766 (14.5)	1389 (26.3)	1805 (34.1)	643 (12.2)
	Highly likely Bacterial Pneumonia	141	1 (0.7)	3 (2.1)	15 (10.6)	24 (17.0)	37 (26.2)	37 (26.2)	21 (14.9)	3 (2.1)

Percentage values are row percentages

Supplementary table 4 - Organ specific complications stratified by age and presence of comorbidity in adults admitted to hospital with severe COVID-19 in adults admitted to hospital with severe COVID-19.

Number of existing comorbidities on admission		Total	Age group (years) 19-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
0	Total N (%)	13908	862 (6.2)	1430 (10.3)	2140 (15.4)	2907 (20.9)	2341 (16.8)	1925 (13.8)	1700 (12.2)	603 (4.3)
	Systemic	1614 (11.6)	61 (7.1)	153 (10.7)	245 (11.4)	368 (12.7)	334 (14.3)	233 (12.1)	159 (9.4)	61 (10.1)
	Renal	2170 (15.6)	45 (5.2)	122 (8.5)	273 (12.8)	497 (17.1)	497 (21.2)	365 (19.0)	281 (16.5)	90 (14.9)
	Gastrointestinal	1657 (11.9)	64 (7.4)	162 (11.3)	299 (14.0)	459 (15.8)	320 (13.7)	210 (10.9)	111 (6.5)	32 (5.3)
	Cardiovascular	1046 (7.5)	21 (2.4)	46 (3.2)	134 (6.3)	212 (7.3)	219 (9.4)	199 (10.3)	162 (9.5)	53 (8.8)
	Neurological	409 (2.9)	12 (1.4)	35 (2.4)	52 (2.4)	75 (2.6)	78 (3.3)	65 (3.4)	79 (4.6)	13 (2.2)
	Respiratory	2562 (18.4)	61 (7.1)	185 (12.9)	462 (21.6)	676 (23.3)	596 (25.5)	372 (19.3)	164 (9.6)	46 (7.6)
	Any complication	5328 (38.3)	184 (21.3)	427 (29.9)	816 (38.1)	1184 (40.7)	1059 (45.2)	811 (42.1)	650 (38.2)	197 (32.7)
1	Total N (%)	17635	434 (2.5)	780 (4.4)	1550 (8.8)	2850 (16.2)	3031 (17.2)	3786 (21.5)	3768 (21.4)	1436 (8.1)
	Systemic	2495 (14.1)	49 (11.3)	113 (14.5)	218 (14.1)	439 (15.4)	516 (17.0)	508 (13.4)	468 (12.4)	184 (12.8)
	Renal	3747 (21.2)	42 (9.7)	105 (13.5)	261 (16.8)	603 (21.2)	796 (26.3)	867 (22.9)	795 (21.1)	278 (19.4)
	Gastrointestinal	2021 (11.5)	50 (11.5)	112 (14.4)	235 (15.2)	450 (15.8)	454 (15.0)	380 (10.0)	244 (6.5)	96 (6.7)
	Cardiovascular	1801 (10.2)	14 (3.2)	52 (6.7)	103 (6.6)	255 (8.9)	353 (11.6)	427 (11.3)	417 (11.1)	180 (12.5)
	Neurological	693 (3.9)	17 (3.9)	27 (3.5)	52 (3.4)	105 (3.7)	141 (4.7)	145 (3.8)	155 (4.1)	51 (3.6)
	Respiratory	3416 (19.4)	55 (12.7)	155 (19.9)	331 (21.4)	716 (25.1)	797 (26.3)	707 (18.7)	488 (13.0)	167 (11.6)
	Any complication	8198 (46.5)	142 (32.7)	316 (40.5)	653 (42.1)	1334 (46.8)	1555 (51.3)	1814 (47.9)	1730 (45.9)	654 (45.5)
2+	Total N (%)	41654	204 (0.5)	543 (1.3)	1306 (3.1)	3344 (8.0)	5767 (13.8)	10852 (26.1)	14432 (34.6)	5206 (12.5)
	Systemic	7786 (18.7)	37 (18.1)	110 (20.3)	268 (20.5)	697 (20.8)	1158 (20.1)	1986 (18.3)	2614 (18.1)	916 (17.6)
	Renal	11835 (28.4)	39 (19.1)	126 (23.2)	340 (26.0)	978 (29.2)	1762 (30.6)	3086 (28.4)	4085 (28.3)	1419 (27.3)
	Gastrointestinal	4223 (10.1)	25 (12.3)	91 (16.8)	206 (15.8)	559 (16.7)	804 (13.9)	1054 (9.7)	1123 (7.8)	361 (6.9)
	Cardiovascular	6126 (14.7)	12 (5.9)	36 (6.6)	133 (10.2)	380 (11.4)	817 (14.2)	1594 (14.7)	2309 (16.0)	845 (16.2)
	Neurological	2013 (4.8)	9 (4.4)	29 (5.3)	58 (4.4)	172 (5.1)	281 (4.9)	515 (4.7)	707 (4.9)	242 (4.6)
	Respiratory	7508 (18.0)	29 (14.2)	117 (21.5)	376 (28.8)	871 (26.0)	1374 (23.8)	1899 (17.5)	2109 (14.6)	733 (14.1)
	Any complication	22841 (54.8)	85 (41.7)	272 (50.1)	701 (53.7)	1900 (56.8)	3340 (57.9)	5924 (54.6)	7827 (54.2)	2792 (53.6)

Percentage values are row percentages, except for totals which represent column percentages

Supplementary table 5 - Specific complications stratified by age and presence of comorbidity in adults admitted to hospital with severe COVID-19.

Number of existing comorbidities on admission		Total	Age group (years) 19-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
0	Total N (%)	13908	862 (6.2)	1430 (10.3)	2140 (15.4)	2907 (20.9)	2341 (16.8)	1925 (13.8)	1700 (12.2)	603 (4.3)
	Empyema	12 (0.1)	0 (0.0)	1 (0.1)	2 (0.1)	2 (0.1)	4 (0.2)	2 (0.1)	1 (0.1)	0 (0.0)
	Likely ARDS	2167 (15.6)	44 (5.1)	156 (10.9)	405 (18.9)	593 (20.4)	525 (22.4)	310 (16.1)	113 (6.6)	21 (3.5)
	Pneumothorax	173 (1.2)	9 (1.0)	14 (1.0)	30 (1.4)	51 (1.8)	44 (1.9)	21 (1.1)	2 (0.1)	2 (0.3)
	Pleural effusion	566 (4.1)	21 (2.4)	41 (2.9)	89 (4.2)	122 (4.2)	120 (5.1)	93 (4.8)	56 (3.3)	24 (4.0)
	Highly likely Bacterial Pneumonia	111 (0.8)	1 (0.1)	6 (0.4)	23 (1.1)	39 (1.3)	21 (0.9)	19 (1.0)	2 (0.1)	0 (0.0)
	Meningitis / Encephalitis	41 (0.3)	5 (0.6)	6 (0.4)	6 (0.3)	6 (0.2)	9 (0.4)	4 (0.2)	4 (0.2)	1 (0.2)
	Seizure	106 (0.8)	6 (0.7)	18 (1.3)	18 (0.8)	24 (0.8)	14 (0.6)	12 (0.6)	13 (0.8)	1 (0.2)
	Stroke / Cerebrovascular accident	189 (1.4)	0 (0.0)	7 (0.5)	18 (0.8)	28 (1.0)	42 (1.8)	43 (2.2)	45 (2.6)	6 (1.0)
	Other neurological complication	117 (0.8)	2 (0.2)	7 (0.5)	17 (0.8)	25 (0.9)	26 (1.1)	13 (0.7)	21 (1.2)	6 (1.0)
	Congestive heart failure	111 (0.8)	0 (0.0)	5 (0.3)	7 (0.3)	16 (0.6)	16 (0.7)	23 (1.2)	27 (1.6)	17 (2.8)
	Endocarditis / Myocarditis Pericarditis	52 (0.4)	0 (0.0)	7 (0.5)	10 (0.5)	8 (0.3)	17 (0.7)	6 (0.3)	3 (0.2)	1 (0.2)
	Myocarditis / Pericarditis	41 (0.3)	2 (0.2)	3 (0.2)	11 (0.5)	13 (0.4)	7 (0.3)	2 (0.1)	3 (0.2)	0 (0.0)
	Cardiomyopathy	16 (0.1)	0 (0.0)	2 (0.1)	3 (0.1)	3 (0.1)	5 (0.2)	1 (0.1)	2 (0.1)	0 (0.0)
	Cardiac arrhythmia	672 (4.8)	15 (1.7)	28 (2.0)	90 (4.2)	138 (4.7)	157 (6.7)	130 (6.8)	86 (5.1)	28 (4.6)
	Cardiac ischaemia	84 (0.6)	0 (0.0)	8 (0.6)	7 (0.3)	13 (0.4)	14 (0.6)	16 (0.8)	21 (1.2)	5 (0.8)
	Cardiac arrest	269 (1.9)	7 (0.8)	6 (0.4)	35 (1.6)	54 (1.9)	50 (2.1)	63 (3.3)	44 (2.6)	10 (1.7)
	Bloodstream Infection	193 (1.4)	3 (0.3)	20 (1.4)	36 (1.7)	38 (1.3)	43 (1.8)	26 (1.4)	20 (1.2)	7 (1.2)
	Coagulation disorder / DIC	383 (2.8)	10 (1.2)	40 (2.8)	71 (3.3)	92 (3.2)	79 (3.4)	55 (2.9)	27 (1.6)	9 (1.5)
	Anaemia	1253 (9.0)	53 (6.1)	114 (8.0)	180 (8.4)	288 (9.9)	262 (11.2)	191 (9.9)	116 (6.8)	49 (8.1)
	Rhabdomyolysis / Myositis	45 (0.3)	2 (0.2)	3 (0.2)	8 (0.4)	9 (0.3)	4 (0.2)	8 (0.4)	6 (0.4)	5 (0.8)
	Acute Kidney Injury	2170 (15.6)	45 (5.2)	122 (8.5)	273 (12.8)	497 (17.1)	497 (21.2)	365 (19.0)	281 (16.5)	90 (14.9)
	Gastrointestinal haemorrhage	87 (0.6)	6 (0.7)	5 (0.3)	7 (0.3)	21 (0.7)	21 (0.9)	8 (0.4)	14 (0.8)	5 (0.8)
	Pancreatitis	43 (0.3)	5 (0.6)	10 (0.7)	4 (0.2)	11 (0.4)	5 (0.2)	5 (0.3)	1 (0.1)	2 (0.3)
	Deep Vein Thrombosis	99 (0.7)	2 (0.2)	8 (0.6)	15 (0.7)	31 (1.1)	25 (1.1)	10 (0.5)	6 (0.4)	2 (0.3)
	Pulmonary Embolism	257 (1.8)	5 (0.6)	19 (1.3)	48 (2.2)	78 (2.7)	54 (2.3)	32 (1.7)	19 (1.1)	2 (0.3)
	Liver Injury	1566 (11.3)	58 (6.7)	150 (10.5)	293 (13.7)	440 (15.1)	302 (12.9)	201 (10.4)	97 (5.7)	25 (4.1)
1	Total N (%)	17635	434 (2.5)	780 (4.4)	1550 (8.8)	2850 (16.2)	3031 (17.2)	3786 (21.5)	3768 (21.4)	1436 (8.1)
	Empyema	23 (0.1)	0 (0.0)	3 (0.4)	2 (0.1)	3 (0.1)	6 (0.2)	3 (0.1)	3 (0.1)	3 (0.2)
	Likely ARDS	2653 (15.0)	49 (11.3)	132 (16.9)	293 (18.9)	627 (22.0)	677 (22.3)	526 (13.9)	275 (7.3)	74 (5.2)
	Pneumothorax	208 (1.2)	2 (0.5)	8 (1.0)	22 (1.4)	55 (1.9)	59 (1.9)	41 (1.1)	16 (0.4)	5 (0.3)

Number of existing comorbidities on admission		Total	Age group (years) 19-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
	Pleural effusion	959 (5.4)	10 (2.3)	34 (4.4)	56 (3.6)	129 (4.5)	187 (6.2)	217 (5.7)	226 (6.0)	100 (7.0)
	Highly likely Bacterial Pneumonia	107 (0.6)	1 (0.2)	5 (0.6)	14 (0.9)	40 (1.4)	23 (0.8)	19 (0.5)	4 (0.1)	1 (0.1)
	Meningitis / Encephalitis	33 (0.2)	1 (0.2)	3 (0.4)	3 (0.2)	6 (0.2)	10 (0.3)	7 (0.2)	3 (0.1)	0 (0.0)
	Seizure	178 (1.0)	7 (1.6)	16 (2.1)	26 (1.7)	34 (1.2)	36 (1.2)	20 (0.5)	29 (0.8)	10 (0.7)
	Stroke / Cerebrovascular accident	293 (1.7)	2 (0.5)	3 (0.4)	16 (1.0)	33 (1.2)	55 (1.8)	81 (2.1)	76 (2.0)	27 (1.9)
	Other neurological complication	262 (1.5)	9 (2.1)	11 (1.4)	17 (1.1)	44 (1.5)	51 (1.7)	53 (1.4)	61 (1.6)	16 (1.1)
	Congestive heart failure	316 (1.8)	0 (0.0)	5 (0.6)	9 (0.6)	24 (0.8)	47 (1.6)	78 (2.1)	90 (2.4)	63 (4.4)
	Endocarditis / Myocarditis Pericarditis	70 (0.4)	0 (0.0)	8 (1.0)	6 (0.4)	14 (0.5)	19 (0.6)	13 (0.3)	8 (0.2)	2 (0.1)
	Myocarditis / Pericarditis	53 (0.3)	1 (0.2)	2 (0.3)	8 (0.5)	8 (0.3)	12 (0.4)	13 (0.3)	7 (0.2)	2 (0.1)
	Cardiomyopathy	34 (0.2)	0 (0.0)	1 (0.1)	5 (0.3)	8 (0.3)	5 (0.2)	8 (0.2)	6 (0.2)	1 (0.1)
	Cardiac arrhythmia	1082 (6.1)	12 (2.8)	28 (3.6)	66 (4.3)	159 (5.6)	229 (7.6)	268 (7.1)	231 (6.1)	89 (6.2)
	Cardiac ischaemia	176 (1.0)	0 (0.0)	5 (0.6)	7 (0.5)	23 (0.8)	37 (1.2)	45 (1.2)	43 (1.1)	16 (1.1)
	Cardiac arrest	461 (2.6)	1 (0.2)	16 (2.1)	27 (1.7)	87 (3.1)	96 (3.2)	98 (2.6)	95 (2.5)	41 (2.9)
	Bloodstream Infection	296 (1.7)	9 (2.1)	19 (2.4)	34 (2.2)	58 (2.0)	61 (2.0)	53 (1.4)	48 (1.3)	14 (1.0)
	Coagulation disorder / DIC	489 (2.8)	12 (2.8)	22 (2.8)	51 (3.3)	106 (3.7)	126 (4.2)	96 (2.5)	56 (1.5)	20 (1.4)
	Anaemia	2012 (11.4)	34 (7.8)	92 (11.8)	173 (11.2)	351 (12.3)	419 (13.8)	407 (10.8)	380 (10.1)	156 (10.9)
	Rhabdomyolysis / Myositis	54 (0.3)	4 (0.9)	1 (0.1)	4 (0.3)	9 (0.3)	7 (0.2)	14 (0.4)	13 (0.3)	2 (0.1)
	Acute Kidney Injury	3747 (21.2)	42 (9.7)	105 (13.5)	261 (16.8)	603 (21.2)	796 (26.3)	867 (22.9)	795 (21.1)	278 (19.4)
	Gastrointestinal haemorrhage	187 (1.1)	2 (0.5)	4 (0.5)	21 (1.4)	29 (1.0)	38 (1.3)	29 (0.8)	41 (1.1)	23 (1.6)
	Pancreatitis	67 (0.4)	3 (0.7)	7 (0.9)	10 (0.6)	17 (0.6)	14 (0.5)	8 (0.2)	7 (0.2)	1 (0.1)
	Deep Vein Thrombosis	102 (0.6)	0 (0.0)	2 (0.3)	14 (0.9)	19 (0.7)	26 (0.9)	26 (0.7)	13 (0.3)	2 (0.1)
	Pulmonary Embolism	261 (1.5)	6 (1.4)	6 (0.8)	31 (2.0)	50 (1.8)	64 (2.1)	51 (1.3)	47 (1.2)	6 (0.4)
	Liver Injury	1859 (10.5)	48 (11.1)	105 (13.5)	220 (14.2)	430 (15.1)	425 (14.0)	351 (9.3)	205 (5.4)	75 (5.2)
2+	Total N (%)	41654	204 (0.5)	543 (1.3)	1306 (3.1)	3344 (8.0)	5767 (13.8)	10852 (26.1)	14432 (34.6)	5206 (12.5)
	Empyema	57 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)	8 (0.2)	10 (0.2)	11 (0.1)	18 (0.1)	8 (0.2)
	Likely ARDS	4871 (11.7)	23 (11.3)	106 (19.5)	314 (24.0)	709 (21.2)	1043 (18.1)	1243 (11.5)	1108 (7.7)	325 (6.2)
	Pneumothorax	313 (0.8)	1 (0.5)	9 (1.7)	21 (1.6)	46 (1.4)	75 (1.3)	77 (0.7)	65 (0.5)	19 (0.4)
	Pleural effusion	3006 (7.2)	8 (3.9)	25 (4.6)	85 (6.5)	214 (6.4)	416 (7.2)	743 (6.8)	1085 (7.5)	430 (8.3)
	Highly likely Bacterial Pneumonia	141 (0.3)	1 (0.5)	3 (0.6)	15 (1.1)	24 (0.7)	37 (0.6)	37 (0.3)	21 (0.1)	3 (0.1)
	Meningitis / Encephalitis	82 (0.2)	1 (0.5)	0 (0.0)	12 (0.9)	15 (0.4)	23 (0.4)	9 (0.1)	20 (0.1)	2 (0.0)
	Seizure	545 (1.3)	6 (2.9)	16 (2.9)	24 (1.8)	77 (2.3)	83 (1.4)	152 (1.4)	150 (1.0)	37 (0.7)
	Stroke / Cerebrovascular accident	731 (1.8)	1 (0.5)	7 (1.3)	16 (1.2)	46 (1.4)	117 (2.0)	187 (1.7)	264 (1.8)	93 (1.8)

Number of existing comorbidities on admission		Total	Age group (years) 19-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
	Other neurological complication	856 (2.1)	4 (2.0)	8 (1.5)	19 (1.5)	63 (1.9)	90 (1.6)	214 (2.0)	331 (2.3)	127 (2.4)
	Congestive heart failure	2101 (5.0)	0 (0.0)	6 (1.1)	27 (2.1)	78 (2.3)	214 (3.7)	506 (4.7)	914 (6.3)	356 (6.8)
	Endocarditis / Myocarditis Pericarditis	142 (0.3)	2 (1.0)	2 (0.4)	9 (0.7)	18 (0.5)	27 (0.5)	43 (0.4)	39 (0.3)	2 (0.0)
	Myocarditis / Pericarditis	97 (0.2)	1 (0.5)	2 (0.4)	6 (0.5)	11 (0.3)	19 (0.3)	26 (0.2)	22 (0.2)	10 (0.2)
	Cardiomyopathy	124 (0.3)	0 (0.0)	2 (0.4)	7 (0.5)	12 (0.4)	18 (0.3)	31 (0.3)	42 (0.3)	12 (0.2)
	Cardiac arrhythmia	3098 (7.4)	8 (3.9)	22 (4.1)	74 (5.7)	210 (6.3)	438 (7.6)	824 (7.6)	1129 (7.8)	393 (7.5)
	Cardiac ischaemia	738 (1.8)	0 (0.0)	1 (0.2)	11 (0.8)	49 (1.5)	97 (1.7)	204 (1.9)	261 (1.8)	115 (2.2)
	Cardiac arrest	1173 (2.8)	1 (0.5)	10 (1.8)	31 (2.4)	99 (3.0)	185 (3.2)	327 (3.0)	377 (2.6)	143 (2.7)
	Bloodstream Infection	626 (1.5)	3 (1.5)	12 (2.2)	30 (2.3)	51 (1.5)	109 (1.9)	151 (1.4)	203 (1.4)	67 (1.3)
	Coagulation disorder / DIC	1199 (2.9)	5 (2.5)	19 (3.5)	55 (4.2)	161 (4.8)	202 (3.5)	288 (2.7)	362 (2.5)	107 (2.1)
	Anaemia	6641 (15.9)	33 (16.2)	97 (17.9)	226 (17.3)	586 (17.5)	991 (17.2)	1693 (15.6)	2232 (15.5)	783 (15.0)
	Rhabdomyolysis / Myositis	167 (0.4)	2 (1.0)	3 (0.6)	2 (0.2)	15 (0.4)	18 (0.3)	35 (0.3)	59 (0.4)	33 (0.6)
	Acute Kidney Injury	11835 (28.4)	39 (19.1)	126 (23.2)	340 (26.0)	978 (29.2)	1762 (30.6)	3086 (28.4)	4085 (28.3)	1419 (27.3)
	Gastrointestinal haemorrhage	581 (1.4)	2 (1.0)	8 (1.5)	12 (0.9)	40 (1.2)	80 (1.4)	141 (1.3)	224 (1.6)	74 (1.4)
	Pancreatitis	138 (0.3)	3 (1.5)	10 (1.8)	13 (1.0)	25 (0.7)	26 (0.5)	26 (0.2)	29 (0.2)	6 (0.1)
	Deep Vein Thrombosis	228 (0.5)	1 (0.5)	7 (1.3)	5 (0.4)	40 (1.2)	37 (0.6)	52 (0.5)	66 (0.5)	20 (0.4)
	Pulmonary Embolism	486 (1.2)	3 (1.5)	4 (0.7)	26 (2.0)	76 (2.3)	101 (1.8)	130 (1.2)	120 (0.8)	26 (0.5)
	Liver Injury	3683 (8.8)	22 (10.8)	81 (14.9)	194 (14.9)	530 (15.8)	733 (12.7)	922 (8.5)	915 (6.3)	286 (5.5)

Percentage values are row percentages, except for totals which represent column percentages. ARDS – Acute Respiratory Distress Syndrome, DIC – Disseminated Intravascular Coagulation.

Supplementary table 6 - Outcomes by organ specific complications in adults admitted to hospital with severe COVID-19 who survived.

		Total number of patients experiencing complications		Organ-specific level complications§					
		Total patients	Any complication	Systemic	Renal	Gastrointestinal	Cardiovascular	Neurological	Respiratory
Total N (%)		50105	21784 (43.5)	7423 (14.8)	10059 (20.1)	4837 (9.7)	4035 (8.1)	1880 (3.8)	7028 (14.0)
Critical Care Admission	No	43153 (86.1)	16853 (77.4)	5557 (74.9)	7467 (74.2)	3233 (66.8)	3020 (74.8)	1461 (77.7)	3616 (51.5)
	Yes	6242 (12.5)	4926 (22.6)	1866 (25.1)	2589 (25.7)	1602 (33.1)	1015 (25.2)	419 (22.3)	3410 (48.5)
	(Missing)	710 (1.4)	5 (0.0)	0 (0.0)	3 (0.0)	2 (0.0)	0 (0.0)	0 (0.0)	2 (0.0)
Any invasive ventilation	No	45825 (91.5)	18630 (85.5)	6067 (81.7)	8271 (82.2)	3728 (77.1)	3275 (81.2)	1533 (81.5)	4498 (64.0)
	Yes	3472 (6.9)	3130 (14.4)	1352 (18.2)	1773 (17.6)	1104 (22.8)	758 (18.8)	347 (18.5)	2529 (36.0)
	(Missing)	808 (1.6)	24 (0.1)	4 (0.1)	15 (0.1)	5 (0.1)	2 (0.0)	0 (0.0)	1 (0.0)
Any non-invasive ventilation	No	42350 (87.2)	17255 (80.1)	5917 (80.3)	7738 (77.8)	3568 (74.6)	3184 (79.6)	1566 (84.3)	4232 (60.6)
	Yes	6206 (12.8)	4296 (19.9)	1454 (19.7)	2207 (22.2)	1218 (25.4)	817 (20.4)	291 (15.7)	2748 (39.4)
Any oxygen	No	15507 (31.8)	4892 (22.6)	1748 (23.7)	1942 (19.4)	940 (19.5)	888 (22.2)	580 (31.1)	627 (8.9)
	Yes	33310 (68.2)	16760 (77.4)	5642 (76.3)	8061 (80.6)	3873 (80.5)	3120 (77.8)	1285 (68.9)	6379 (91.1)

Percentage values are row percentages, except for totals which represent column percentages. § = Denominator is number of non-missing observations for each organ system.

Supplementary table 7 - Outcomes by organ specific complications in adults admitted to hospital with severe COVID-19 who died.

		Total number of patients experiencing complications		Organ-specific level complications§					
		Total	Any complication	Systemic	Renal	Gastrointestinal	Cardiovascular	Neurological	Respiratory
Total N (%)		23092	14583 (63.2)	4472 (19.4)	7693 (33.3)	3064 (13.3)	4938 (21.4)	1235 (5.3)	6458 (28.0)
Critical Care Admission	No	18972 (82.2)	11239 (77.1)	3247 (72.6)	5525 (71.8)	1906 (62.2)	3620 (73.3)	985 (79.8)	3856 (59.7)
	Yes	3792 (16.4)	3341 (22.9)	1224 (27.4)	2166 (28.2)	1158 (37.8)	1318 (26.7)	249 (20.2)	2602 (40.3)
	(Missing)	328 (1.4)	3 (0.0)	1 (0.0)	2 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
Any invasive ventilation	No	20063 (86.9)	12080 (82.8)	3489 (78.0)	5991 (77.9)	2087 (68.1)	3911 (79.2)	1040 (84.2)	4311 (66.8)
	Yes	2650 (11.5)	2489 (17.1)	978 (21.9)	1698 (22.1)	973 (31.8)	1026 (20.8)	195 (15.8)	2141 (33.2)
	(Missing)	379 (1.6)	14 (0.1)	5 (0.1)	4 (0.1)	4 (0.1)	1 (0.0)	0 (0.0)	6 (0.1)
Any non-invasive ventilation	No	17685 (79.3)	10947 (76.1)	3311 (74.8)	5623 (73.9)	2117 (70.0)	3678 (75.1)	1000 (81.8)	4100 (64.2)
	Yes	4621 (20.7)	3445 (23.9)	1113 (25.2)	1987 (26.1)	906 (30.0)	1217 (24.9)	222 (18.2)	2290 (35.8)
Any oxygen	No	2145 (9.5)	1079 (7.4)	331 (7.4)	528 (6.9)	213 (7.0)	302 (6.1)	157 (12.8)	211 (3.3)
	Yes	20385 (90.5)	13421 (92.6)	4120 (92.6)	7128 (93.1)	2832 (93.0)	4624 (93.9)	1073 (87.2)	6219 (96.7)

Percentage values are row percentages, except for totals which represent column percentages. § = Denominator is number of non-missing observations for each organ system.

Supplementary table 8 - Effect of complications on survival (adjusted Cox proportional hazards models) for figure 2C

Supplementary table 8A - Any complication

Dependent: Survival (mortality)			HR (univariable)	HR (multivariable)
Any complication	No	37839 (100.0)	-	-
	Yes	36662 (100.0)	1.91 (1.86-1.97, p<0.001)	1.74 (1.64-1.84, p<0.001)
Age on admission	19-29	1477 (100.0)	-	-
	30-39	2707 (100.0)	1.82 (1.25-2.64, p=0.002)	1.68 (1.22-2.31, p=0.002)
	40-49	4930 (100.0)	3.22 (2.29-4.53, p<0.001)	2.78 (1.97-3.94, p<0.001)
	50-59	9003 (100.0)	6.24 (4.48-8.68, p<0.001)	5.26 (3.79-7.29, p<0.001)
	60-69	11035 (100.0)	11.72 (8.43-16.27, p<0.001)	9.68 (6.99-13.40, p<0.001)
	70-79	16445 (100.0)	18.38 (13.25-25.51, p<0.001)	15.44 (11.07-21.54, p<0.001)
	80-89	19771 (100.0)	23.49 (16.93-32.59, p<0.001)	20.15 (14.56-27.89, p<0.001)
	90+	7204 (100.0)	27.63 (19.89-38.36, p<0.001)	24.73 (17.77-34.40, p<0.001)
Sex at Birth	Female	31733 (100.0)	-	-
	Male	40648 (100.0)	1.23 (1.20-1.27, p<0.001)	1.30 (1.26-1.33, p<0.001)
Deprivation	1 (least deprived)	10347 (100.0)	-	-
	2	12775 (100.0)	1.00 (0.96-1.05, p=0.965)	1.03 (0.97-1.08, p=0.348)
	3	15712 (100.0)	0.99 (0.95-1.04, p=0.743)	1.06 (0.99-1.12, p=0.074)
	4	15880 (100.0)	0.95 (0.91-1.00, p=0.039)	1.07 (1.01-1.13, p=0.033)
	5 (most deprived)	17845 (100.0)	0.93 (0.89-0.97, p=0.001)	1.09 (1.03-1.15, p=0.002)

Supplementary table 8B - Systemic complications

Dependent: Survival (mortality)			HR (univariable)	HR (multivariable)
Systemic Complication	No	62531 (100.0)	-	-
	Yes	11970 (100.0)	1.27 (1.23-1.31, p<0.001)	1.20 (1.15-1.26, p<0.001)
Age on admission	19-29	1477 (100.0)	-	-
	30-39	2707 (100.0)	1.82 (1.25-2.64, p=0.002)	1.75 (1.27-2.42, p=0.001)
	40-49	4930 (100.0)	3.22 (2.29-4.53, p<0.001)	3.00 (2.12-4.26, p<0.001)
	50-59	9003 (100.0)	6.24 (4.48-8.68, p<0.001)	5.79 (4.17-8.04, p<0.001)
	60-69	11035 (100.0)	11.72 (8.43-16.27, p<0.001)	10.87 (7.84-15.07, p<0.001)
	70-79	16445 (100.0)	18.38 (13.25-25.51, p<0.001)	17.25 (12.36-24.09, p<0.001)
	80-89	19771 (100.0)	23.49 (16.93-32.59, p<0.001)	22.50 (16.24-31.18, p<0.001)
	90+	7204 (100.0)	27.63 (19.89-38.36, p<0.001)	27.61 (19.83-38.43, p<0.001)
Sex at Birth	Female	31733 (100.0)	-	-
	Male	40648 (100.0)	1.23 (1.20-1.27, p<0.001)	1.34 (1.30-1.38, p<0.001)
Deprivation	1 (least deprived)	10347 (100.0)	-	-
	2	12775 (100.0)	1.00 (0.96-1.05, p=0.965)	1.03 (0.98-1.08, p=0.281)
	3	15712 (100.0)	0.99 (0.95-1.04, p=0.743)	1.06 (1.00-1.12, p=0.059)
	4	15880 (100.0)	0.95 (0.91-1.00, p=0.039)	1.07 (1.02-1.13, p=0.012)
	5 (most deprived)	17845 (100.0)	0.93 (0.89-0.97, p=0.001)	1.09 (1.04-1.15, p=0.001)

Supplementary table 8C - Renal complications/ acute kidney injury

Dependent: Survival (mortality)			HR (univariable)	HR (multivariable)
Renal complication	No	56691 (100.0)	-	-
	Yes	17810 (100.0)	1.68 (1.64-1.73, p<0.001)	1.49 (1.42-1.55, p<0.001)
Age on admission	19-29	1477 (100.0)	-	-
	30-39	2707 (100.0)	1.82 (1.25-2.64, p=0.002)	1.74 (1.26-2.39, p=0.001)
	40-49	4930 (100.0)	3.22 (2.29-4.53, p<0.001)	2.92 (2.06-4.14, p<0.001)
	50-59	9003 (100.0)	6.24 (4.48-8.68, p<0.001)	5.53 (3.99-7.68, p<0.001)
	60-69	11035 (100.0)	11.72 (8.43-16.27, p<0.001)	10.22 (7.37-14.17, p<0.001)
	70-79	16445 (100.0)	18.38 (13.25-25.51, p<0.001)	16.24 (11.63-22.67, p<0.001)
	80-89	19771 (100.0)	23.49 (16.93-32.59, p<0.001)	21.16 (15.27-29.32, p<0.001)
	90+	7204 (100.0)	27.63 (19.89-38.36, p<0.001)	26.05 (18.70-36.27, p<0.001)
Sex at Birth	Female	31733 (100.0)	-	-
	Male	40648 (100.0)	1.23 (1.20-1.27, p<0.001)	1.31 (1.27-1.35, p<0.001)
Deprivation	1 (least deprived)	10347 (100.0)	-	-
	2	12775 (100.0)	1.00 (0.96-1.05, p=0.965)	1.03 (0.98-1.08, p=0.317)
	3	15712 (100.0)	0.99 (0.95-1.04, p=0.743)	1.05 (0.99-1.11, p=0.089)
	4	15880 (100.0)	0.95 (0.91-1.00, p=0.039)	1.06 (1.00-1.12, p=0.046)
	5 (most deprived)	17845 (100.0)	0.93 (0.89-0.97, p=0.001)	1.08 (1.02-1.13, p=0.006)

Supplementary table 8D - Gastrointestinal and liver complications

Dependent: Survival (mortality)			HR (univariable)	HR (multivariable)
Gastrointestinal or liver complication	No	66464 (100.0)	-	-
	Yes	8037 (100.0)	1.28 (1.23-1.33, p<0.001)	1.50 (1.44-1.57, p<0.001)
Age on admission	18-29	1477 (100.0)	-	-
	30-39	2707 (100.0)	1.82 (1.25-2.64, p=0.002)	1.74 (1.26-2.39, p=0.001)
	40-49	4930 (100.0)	3.22 (2.29-4.53, p<0.001)	2.97 (2.10-4.20, p<0.001)
	50-59	9003 (100.0)	6.24 (4.48-8.68, p<0.001)	5.71 (4.12-7.92, p<0.001)
	60-69	11035 (100.0)	11.72 (8.43-16.27, p<0.001)	10.85 (7.84-15.02, p<0.001)
	70-79	16445 (100.0)	18.38 (13.25-25.51, p<0.001)	17.54 (12.58-24.45, p<0.001)
	80-89	19771 (100.0)	23.49 (16.93-32.59, p<0.001)	23.15 (16.73-32.03, p<0.001)
	90+	7204 (100.0)	27.63 (19.89-38.36, p<0.001)	28.46 (20.46-39.59, p<0.001)
Sex at Birth	Female	31733 (100.0)	-	-
	Male	40648 (100.0)	1.23 (1.20-1.27, p<0.001)	1.33 (1.29-1.37, p<0.001)
Deprivation	1 (least deprived)	10347 (100.0)	-	-
	2	12775 (100.0)	1.00 (0.96-1.05, p=0.965)	1.03 (0.98-1.08, p=0.292)
	3	15712 (100.0)	0.99 (0.95-1.04, p=0.743)	1.06 (1.00-1.12, p=0.052)
	4	15880 (100.0)	0.95 (0.91-1.00, p=0.039)	1.08 (1.02-1.14, p=0.011)
	5 (most deprived)	17845 (100.0)	0.93 (0.89-0.97, p=0.001)	1.09 (1.04-1.15, p=0.001)

63 *Supplementary table 8E - Cardiovascular complications*

Dependent: Survival (mortality)			HR (univariable)	HR (multivariable)
Cardiovascular complication	No	65498 (100.0)	-	-
	Yes	9003 (100.0)	2.32 (2.25-2.39, p<0.001)	1.98 (1.85-2.11, p<0.001)
Age on admission	19-29	1477 (100.0)	-	-
	30-39	2707 (100.0)	1.82 (1.25-2.64, p=0.002)	1.74 (1.26-2.39, p=0.001)
	40-49	4930 (100.0)	3.22 (2.29-4.53, p<0.001)	2.93 (2.07-4.15, p<0.001)
	50-59	9003 (100.0)	6.24 (4.48-8.68, p<0.001)	5.57 (4.02-7.73, p<0.001)
	60-69	11035 (100.0)	11.72 (8.43-16.27, p<0.001)	10.23 (7.38-14.17, p<0.001)
	70-79	16445 (100.0)	18.38 (13.25-25.51, p<0.001)	16.11 (11.55-22.48, p<0.001)
	80-89	19771 (100.0)	23.49 (16.93-32.59, p<0.001)	20.85 (15.05-28.88, p<0.001)
	90+	7204 (100.0)	27.63 (19.89-38.36, p<0.001)	25.50 (18.34-35.45, p<0.001)
Sex at Birth	Female	31733 (100.0)	-	-
	Male	40648 (100.0)	1.23 (1.20-1.27, p<0.001)	1.32 (1.28-1.36, p<0.001)
Deprivation	1 (least deprived)	10347 (100.0)	-	-
	2	12775 (100.0)	1.00 (0.96-1.05, p=0.965)	1.03 (0.98-1.09, p=0.219)
	3	15712 (100.0)	0.99 (0.95-1.04, p=0.743)	1.06 (1.00-1.12, p=0.053)
	4	15880 (100.0)	0.95 (0.91-1.00, p=0.039)	1.07 (1.02-1.14, p=0.012)
	5 (most deprived)	17845 (100.0)	0.93 (0.89-0.97, p=0.001)	1.10 (1.05-1.16, p<0.001)

64

Supplementary table 8F - Neurological complications

Dependent: Survival (mortality)			HR (univariable)	HR (multivariable)
Neurological complication	No	71340 (100.0)	-	-
	Yes	3161 (100.0)	1.29 (1.22-1.37, p<0.001)	1.21 (1.13-1.29, p<0.001)
Age on admission	19-29	1477 (100.0)	-	-
	30-39	2707 (100.0)	1.82 (1.25-2.64, p=0.002)	1.76 (1.28-2.43, p=0.001)
	40-49	4930 (100.0)	3.22 (2.29-4.53, p<0.001)	3.03 (2.13-4.29, p<0.001)
	50-59	9003 (100.0)	6.24 (4.48-8.68, p<0.001)	5.84 (4.21-8.11, p<0.001)
	60-69	11035 (100.0)	11.72 (8.43-16.27, p<0.001)	10.99 (7.93-15.24, p<0.001)
	70-79	16445 (100.0)	18.38 (13.25-25.51, p<0.001)	17.42 (12.48-24.31, p<0.001)
	80-89	19771 (100.0)	23.49 (16.93-32.59, p<0.001)	22.70 (16.38-31.44, p<0.001)
	90+	7204 (100.0)	27.63 (19.89-38.36, p<0.001)	27.85 (20.00-38.77, p<0.001)
Sex at Birth	Female	31733 (100.0)	-	-
	Male	40648 (100.0)	1.23 (1.20-1.27, p<0.001)	1.34 (1.31-1.38, p<0.001)
Deprivation	1 (least deprived)	10347 (100.0)	-	-
	2	12775 (100.0)	1.00 (0.96-1.05, p=0.965)	1.03 (0.98-1.08, p=0.287)
	3	15712 (100.0)	0.99 (0.95-1.04, p=0.743)	1.06 (1.00-1.12, p=0.060)
	4	15880 (100.0)	0.95 (0.91-1.00, p=0.039)	1.07 (1.01-1.13, p=0.014)
	5 (most deprived)	17845 (100.0)	0.93 (0.89-0.97, p=0.001)	1.09 (1.03-1.14, p=0.001)

Supplementary table 8G - Respiratory complications

Dependent: Survival (mortality)			HR (univariable)	HR (multivariable)
Respiratory complication	No	60982 (100.0)	-	-
	Yes	13519 (100.0)	1.89 (1.83-1.94, p<0.001)	2.15 (2.04-2.27, p<0.001)
Age on admission	19-29	1477 (100.0)	-	-
	30-39	2707 (100.0)	1.82 (1.25-2.64, p=0.002)	1.65 (1.20-2.27, p=0.002)
	40-49	4930 (100.0)	3.22 (2.29-4.53, p<0.001)	2.67 (1.89-3.78, p<0.001)
	50-59	9003 (100.0)	6.24 (4.48-8.68, p<0.001)	5.12 (3.70-7.10, p<0.001)
	60-69	11035 (100.0)	11.72 (8.43-16.27, p<0.001)	9.71 (7.01-13.45, p<0.001)
	70-79	16445 (100.0)	18.38 (13.25-25.51, p<0.001)	16.45 (11.80-22.92, p<0.001)
	80-89	19771 (100.0)	23.49 (16.93-32.59, p<0.001)	22.33 (16.15-30.89, p<0.001)
	90+	7204 (100.0)	27.63 (19.89-38.36, p<0.001)	27.49 (19.78-38.21, p<0.001)
Sex at Birth	Female	31733 (100.0)	-	-
	Male	40648 (100.0)	1.23 (1.20-1.27, p<0.001)	1.31 (1.27-1.35, p<0.001)
Deprivation	1 (least deprived)	10347 (100.0)	-	-
	2	12775 (100.0)	1.00 (0.96-1.05, p=0.965)	1.03 (0.98-1.08, p=0.209)
	3	15712 (100.0)	0.99 (0.95-1.04, p=0.743)	1.05 (0.99-1.11, p=0.135)
	4	15880 (100.0)	0.95 (0.91-1.00, p=0.039)	1.07 (1.01-1.13, p=0.022)
	5 (most deprived)	17845 (100.0)	0.93 (0.89-0.97, p=0.001)	1.10 (1.04-1.16, p<0.001)

Supplementary table 9 - Effect of complications on odds of critical care admission (adjusted logistic regression models) for figure 2D

Supplementary table 9A - Any complication

Dependent: Critical Care Admission		No	Yes	OR (univariable)	OR (multilevel)
Any complication	No	33809 (95.1)	1760 (4.9)	-	-
	Yes	27937 (77.4)	8155 (22.6)	5.61 (5.31-5.92, p<0.001)	7.25 (6.83-7.69, p<0.001)
Age on admission	19-29	1241 (85.8)	205 (14.2)	-	-
	30-39	2101 (79.1)	555 (20.9)	1.60 (1.34-1.91, p<0.001)	1.33 (1.10-1.61, p=0.004)
	40-49	3596 (74.0)	1264 (26.0)	2.13 (1.82-2.51, p<0.001)	1.57 (1.32-1.88, p<0.001)
	50-59	6389 (71.7)	2521 (28.3)	2.39 (2.05-2.80, p<0.001)	1.63 (1.38-1.94, p<0.001)
	60-69	8166 (74.9)	2740 (25.1)	2.03 (1.75-2.38, p<0.001)	1.24 (1.04-1.47, p=0.014)
	70-79	14285 (87.9)	1960 (12.1)	0.83 (0.71-0.97, p=0.019)	0.47 (0.39-0.56, p<0.001)
	80-89	18964 (97.1)	567 (2.9)	0.18 (0.15-0.21, p<0.001)	0.10 (0.08-0.12, p<0.001)
	90+	7004 (98.6)	103 (1.4)	0.09 (0.07-0.11, p<0.001)	0.05 (0.04-0.07, p<0.001)
Sex at Birth	Female	28230 (90.1)	3100 (9.9)	-	-
	Male	33348 (83.1)	6792 (16.9)	1.85 (1.77-1.94, p<0.001)	1.49 (1.42-1.57, p<0.001)
Deprivation	1 (least deprived)	8747 (86.2)	1401 (13.8)	-	-
	2	10923 (86.9)	1653 (13.1)	0.94 (0.88-1.02, p=0.146)	0.86 (0.79-0.94, p=0.001)
	3	13352 (86.3)	2115 (13.7)	0.99 (0.92-1.06, p=0.765)	0.89 (0.82-0.98, p=0.012)
	4	13360 (85.1)	2340 (14.9)	1.09 (1.02-1.17, p=0.014)	0.89 (0.82-0.97, p=0.011)
	5 (most deprived)	15352 (86.5)	2405 (13.5)	0.98 (0.91-1.05, p=0.540)	0.78 (0.72-0.85, p<0.001)

Supplementary table 9B - Systemic complications

Dependent: Critical Care Admission		No	Yes	OR (univariable)	OR (multilevel)
Systemic complication	No	53004 (88.5)	6875 (11.5)	-	-
	Yes	8742 (74.2)	3040 (25.8)	2.68 (2.55-2.81, p<0.001)	3.15 (2.97-3.33, p<0.001)
Age on admission	19-29	1241 (85.8)	205 (14.2)	-	-
	30-39	2101 (79.1)	555 (20.9)	1.60 (1.34-1.91, p<0.001)	1.45 (1.21-1.74, p<0.001)
	40-49	3596 (74.0)	1264 (26.0)	2.13 (1.82-2.51, p<0.001)	1.84 (1.56-2.18, p<0.001)
	50-59	6389 (71.7)	2521 (28.3)	2.39 (2.05-2.80, p<0.001)	2.05 (1.74-2.41, p<0.001)
	60-69	8166 (74.9)	2740 (25.1)	2.03 (1.75-2.38, p<0.001)	1.70 (1.45-2.00, p<0.001)
	70-79	14285 (87.9)	1960 (12.1)	0.83 (0.71-0.97, p=0.019)	0.69 (0.58-0.81, p<0.001)
	80-89	18964 (97.1)	567 (2.9)	0.18 (0.15-0.21, p<0.001)	0.15 (0.13-0.18, p<0.001)
	90+	7004 (98.6)	103 (1.4)	0.09 (0.07-0.11, p<0.001)	0.08 (0.06-0.10, p<0.001)
Sex at Birth	Female	28230 (90.1)	3100 (9.9)	-	-
	Male	33348 (83.1)	6792 (16.9)	1.85 (1.77-1.94, p<0.001)	1.65 (1.58-1.74, p<0.001)
Deprivation	1 (least deprived)	8747 (86.2)	1401 (13.8)	-	-
	2	10923 (86.9)	1653 (13.1)	0.94 (0.88-1.02, p=0.146)	0.88 (0.81-0.96, p=0.005)
	3	13352 (86.3)	2115 (13.7)	0.99 (0.92-1.06, p=0.765)	0.90 (0.83-0.98, p=0.020)
	4	13360 (85.1)	2340 (14.9)	1.09 (1.02-1.17, p=0.014)	0.91 (0.84-0.99, p=0.035)
	5 (most deprived)	15352 (86.5)	2405 (13.5)	0.98 (0.91-1.05, p=0.540)	0.82 (0.75-0.89, p<0.001)

Supplementary table 9C - Renal complications/ acute kidney injury

Dependent: Critical Care Admission		No	Yes	OR (univariable)	OR (multilevel)
Renal complication	No	48812 (90.3)	5238 (9.7)	-	-
	Yes	12934 (73.4)	4677 (26.6)	3.37 (3.22-3.52, p<0.001)	4.36 (4.14-4.58, p<0.001)
Age on admission	19-29	1241 (85.8)	205 (14.2)	-	-
	30-39	2101 (79.1)	555 (20.9)	1.60 (1.34-1.91, p<0.001)	1.45 (1.21-1.74, p<0.001)
	40-49	3596 (74.0)	1264 (26.0)	2.13 (1.82-2.51, p<0.001)	1.74 (1.47-2.06, p<0.001)
	50-59	6389 (71.7)	2521 (28.3)	2.39 (2.05-2.80, p<0.001)	1.82 (1.54-2.14, p<0.001)
	60-69	8166 (74.9)	2740 (25.1)	2.03 (1.75-2.38, p<0.001)	1.40 (1.19-1.65, p<0.001)
	70-79	14285 (87.9)	1960 (12.1)	0.83 (0.71-0.97, p=0.019)	0.54 (0.46-0.64, p<0.001)
	80-89	18964 (97.1)	567 (2.9)	0.18 (0.15-0.21, p<0.001)	0.11 (0.10-0.14, p<0.001)
	90+	7004 (98.6)	103 (1.4)	0.09 (0.07-0.11, p<0.001)	0.06 (0.05-0.07, p<0.001)
Sex at Birth	Female	28230 (90.1)	3100 (9.9)	-	-
	Male	33348 (83.1)	6792 (16.9)	1.85 (1.77-1.94, p<0.001)	1.51 (1.44-1.59, p<0.001)
Deprivation	1 (least deprived)	8747 (86.2)	1401 (13.8)	-	-
	2	10923 (86.9)	1653 (13.1)	0.94 (0.88-1.02, p=0.146)	0.89 (0.81-0.97, p=0.009)
	3	13352 (86.3)	2115 (13.7)	0.99 (0.92-1.06, p=0.765)	0.89 (0.82-0.97, p=0.011)
	4	13360 (85.1)	2340 (14.9)	1.09 (1.02-1.17, p=0.014)	0.89 (0.81-0.97, p=0.006)
	5 (most deprived)	15352 (86.5)	2405 (13.5)	0.98 (0.91-1.05, p=0.540)	0.79 (0.73-0.86, p<0.001)

Supplementary table 9D - Gastrointestinal and liver complications

Dependent: Critical Care Admission		No	Yes	OR (univariable)	OR (multilevel)
Gastrointestinal or liver complication	No	56625 (88.8)	7173 (11.2)	-	-
	Yes	5121 (65.1)	2742 (34.9)	4.23 (4.01-4.45, p<0.001)	3.52 (3.32-3.74, p<0.001)
Age on admission	19-29	1241 (85.8)	205 (14.2)	-	-
	30-39	2101 (79.1)	555 (20.9)	1.60 (1.34-1.91, p<0.001)	1.45 (1.21-1.75, p<0.001)
	40-49	3596 (74.0)	1264 (26.0)	2.13 (1.82-2.51, p<0.001)	1.84 (1.56-2.19, p<0.001)
	50-59	6389 (71.7)	2521 (28.3)	2.39 (2.05-2.80, p<0.001)	2.08 (1.77-2.45, p<0.001)
	60-69	8166 (74.9)	2740 (25.1)	2.03 (1.75-2.38, p<0.001)	1.82 (1.55-2.14, p<0.001)
	70-79	14285 (87.9)	1960 (12.1)	0.83 (0.71-0.97, p=0.019)	0.77 (0.65-0.90, p=0.001)
	80-89	18964 (97.1)	567 (2.9)	0.18 (0.15-0.21, p<0.001)	0.18 (0.15-0.21, p<0.001)
	90+	7004 (98.6)	103 (1.4)	0.09 (0.07-0.11, p<0.001)	0.09 (0.07-0.12, p<0.001)
Sex at Birth	Female	28230 (90.1)	3100 (9.9)	-	-
	Male	33348 (83.1)	6792 (16.9)	1.85 (1.77-1.94, p<0.001)	1.56 (1.48-1.63, p<0.001)
Deprivation	1 (least deprived)	8747 (86.2)	1401 (13.8)	-	-
	2	10923 (86.9)	1653 (13.1)	0.94 (0.88-1.02, p=0.146)	0.89 (0.82-0.97, p=0.009)
	3	13352 (86.3)	2115 (13.7)	0.99 (0.92-1.06, p=0.765)	0.93 (0.86-1.01, p=0.096)
	4	13360 (85.1)	2340 (14.9)	1.09 (1.02-1.17, p=0.014)	0.94 (0.87-1.03, p=0.170)
	5 (most deprived)	15352 (86.5)	2405 (13.5)	0.98 (0.91-1.05, p=0.540)	0.85 (0.78-0.92, p<0.001)

Supplementary table 9E - Cardiovascular complications

Dependent: Critical Care Admission		No	Yes	OR (univariable)	OR (multilevel)
Cardiovascular complication	No	55139 (87.9)	7619 (12.1)	-	-
	Yes	6607 (74.2)	2296 (25.8)	2.51 (2.38-2.65, p<0.001)	3.64 (3.42-3.88, p<0.001)
Age on admission	19-29	1241 (85.8)	205 (14.2)	-	-
	30-39	2101 (79.1)	555 (20.9)	1.60 (1.34-1.91, p<0.001)	1.48 (1.24-1.78, p<0.001)
	40-49	3596 (74.0)	1264 (26.0)	2.13 (1.82-2.51, p<0.001)	1.83 (1.54-2.16, p<0.001)
	50-59	6389 (71.7)	2521 (28.3)	2.39 (2.05-2.80, p<0.001)	2.02 (1.72-2.37, p<0.001)
	60-69	8166 (74.9)	2740 (25.1)	2.03 (1.75-2.38, p<0.001)	1.63 (1.39-1.91, p<0.001)
	70-79	14285 (87.9)	1960 (12.1)	0.83 (0.71-0.97, p=0.019)	0.63 (0.53-0.74, p<0.001)
	80-89	18964 (97.1)	567 (2.9)	0.18 (0.15-0.21, p<0.001)	0.13 (0.11-0.16, p<0.001)
	90+	7004 (98.6)	103 (1.4)	0.09 (0.07-0.11, p<0.001)	0.07 (0.05-0.09, p<0.001)
Sex at Birth	Female	28230 (90.1)	3100 (9.9)	-	-
	Male	33348 (83.1)	6792 (16.9)	1.85 (1.77-1.94, p<0.001)	1.61 (1.53-1.69, p<0.001)
Deprivation	1 (least deprived)	8747 (86.2)	1401 (13.8)	-	-
	2	10923 (86.9)	1653 (13.1)	0.94 (0.88-1.02, p=0.146)	0.89 (0.81-0.97, p=0.006)
	3	13352 (86.3)	2115 (13.7)	0.99 (0.92-1.06, p=0.765)	0.92 (0.84-1.00, p=0.046)
	4	13360 (85.1)	2340 (14.9)	1.09 (1.02-1.17, p=0.014)	0.92 (0.85-1.00, p=0.050)
	5 (most deprived)	15352 (86.5)	2405 (13.5)	0.98 (0.91-1.05, p=0.540)	0.83 (0.76-0.90, p<0.001)

Supplementary table 9F - Neurological complications

Dependent: Critical Care Admission		No	Yes	OR (univariable)	OR (multilevel)
Neurological complication	No	59321 (86.5)	9264 (13.5)	-	-
	Yes	2425 (78.8)	651 (21.2)	1.72 (1.57-1.88, p<0.001)	1.88 (1.70-2.08, p<0.001)
Age on admission	19-29	1241 (85.8)	205 (14.2)	-	-
	30-39	2101 (79.1)	555 (20.9)	1.60 (1.34-1.91, p<0.001)	1.51 (1.26-1.81, p<0.001)
	40-49	3596 (74.0)	1264 (26.0)	2.13 (1.82-2.51, p<0.001)	1.91 (1.62-2.26, p<0.001)
	50-59	6389 (71.7)	2521 (28.3)	2.39 (2.05-2.80, p<0.001)	2.17 (1.85-2.55, p<0.001)
	60-69	8166 (74.9)	2740 (25.1)	2.03 (1.75-2.38, p<0.001)	1.85 (1.58-2.17, p<0.001)
	70-79	14285 (87.9)	1960 (12.1)	0.83 (0.71-0.97, p=0.019)	0.75 (0.64-0.88, p<0.001)
	80-89	18964 (97.1)	567 (2.9)	0.18 (0.15-0.21, p<0.001)	0.17 (0.14-0.20, p<0.001)
	90+	7004 (98.6)	103 (1.4)	0.09 (0.07-0.11, p<0.001)	0.09 (0.07-0.11, p<0.001)
Sex at Birth	Female	28230 (90.1)	3100 (9.9)	-	-
	Male	33348 (83.1)	6792 (16.9)	1.85 (1.77-1.94, p<0.001)	1.65 (1.57-1.73, p<0.001)
Deprivation	1 (least deprived)	8747 (86.2)	1401 (13.8)	-	-
	2	10923 (86.9)	1653 (13.1)	0.94 (0.88-1.02, p=0.146)	0.90 (0.82-0.97, p=0.010)
	3	13352 (86.3)	2115 (13.7)	0.99 (0.92-1.06, p=0.765)	0.92 (0.85-1.00, p=0.065)
	4	13360 (85.1)	2340 (14.9)	1.09 (1.02-1.17, p=0.014)	0.94 (0.86-1.02, p=0.114)
	5 (most deprived)	15352 (86.5)	2405 (13.5)	0.98 (0.91-1.05, p=0.540)	0.83 (0.77-0.91, p<0.001)

Supplementary table 9G - Respiratory complications

Dependent: Critical Care Admission		No	Yes	OR (univariable)	OR (multilevel)
Respiratory complication	No	54321 (93.2)	3986 (6.8)	-	-
	Yes	7425 (55.6)	5929 (44.4)	10.88 (10.38-11.41, p<0.001)	12.48 (11.81-13.18, p<0.001)
Age on admission	19-29	1241 (85.8)	205 (14.2)	-	-
	30-39	2101 (79.1)	555 (20.9)	1.60 (1.34-1.91, p<0.001)	1.28 (1.05-1.56, p=0.015)
	40-49	3596 (74.0)	1264 (26.0)	2.13 (1.82-2.51, p<0.001)	1.40 (1.17-1.68, p<0.001)
	50-59	6389 (71.7)	2521 (28.3)	2.39 (2.05-2.80, p<0.001)	1.56 (1.31-1.86, p<0.001)
	60-69	8166 (74.9)	2740 (25.1)	2.03 (1.75-2.38, p<0.001)	1.27 (1.06-1.51, p=0.008)
	70-79	14285 (87.9)	1960 (12.1)	0.83 (0.71-0.97, p=0.019)	0.52 (0.44-0.62, p<0.001)
	80-89	18964 (97.1)	567 (2.9)	0.18 (0.15-0.21, p<0.001)	0.11 (0.09-0.14, p<0.001)
	90+	7004 (98.6)	103 (1.4)	0.09 (0.07-0.11, p<0.001)	0.06 (0.04-0.08, p<0.001)
Sex at Birth	Female	28230 (90.1)	3100 (9.9)	-	-
	Male	33348 (83.1)	6792 (16.9)	1.85 (1.77-1.94, p<0.001)	1.53 (1.44-1.61, p<0.001)
Deprivation	1 (least deprived)	8747 (86.2)	1401 (13.8)	-	-
	2	10923 (86.9)	1653 (13.1)	0.94 (0.88-1.02, p=0.146)	0.86 (0.79-0.95, p=0.003)
	3	13352 (86.3)	2115 (13.7)	0.99 (0.92-1.06, p=0.765)	0.90 (0.82-0.99, p=0.029)
	4	13360 (85.1)	2340 (14.9)	1.09 (1.02-1.17, p=0.014)	0.88 (0.81-0.97, p=0.009)
	5 (most deprived)	15352 (86.5)	2405 (13.5)	0.98 (0.91-1.05, p=0.540)	0.80 (0.73-0.88, p<0.001)

Supplementary table 10 - Effect of complications on odds of worse ability to self-care at discharge (adjusted logistic regression models) for figure 4C

Supplementary table 10A - Any complication

Dependent: Self-care ability		Equivalent to before illness	Worse	OR (univariable)	OR (multilevel)
Any complication	No	19692 (77.4)	5759 (22.6)	-	-
	Yes	12174 (61.7)	7550 (38.3)	2.12 (2.04-2.21, p<0.001)	2.41 (2.30-2.52, p<0.001)
Age (years)	19-29	1121 (86.7)	172 (13.3)	-	-
	30-39	1962 (83.7)	383 (16.3)	1.27 (1.05-1.55, p=0.015)	1.54 (1.24-1.92, p<0.001)
	40-49	3331 (79.9)	838 (20.1)	1.64 (1.38-1.96, p<0.001)	2.03 (1.66-2.48, p<0.001)
	50-59	5508 (78.8)	1486 (21.2)	1.76 (1.49-2.09, p<0.001)	2.22 (1.82-2.69, p<0.001)
	60-69	5451 (73.3)	1990 (26.7)	2.38 (2.02-2.82, p<0.001)	3.02 (2.49-3.66, p<0.001)
	70-79	6237 (66.5)	3139 (33.5)	3.28 (2.79-3.88, p<0.001)	4.18 (3.46-5.06, p<0.001)
	80-89	6069 (61.4)	3810 (38.6)	4.09 (3.48-4.84, p<0.001)	5.38 (4.45-6.50, p<0.001)
	90+	1940 (58.5)	1377 (41.5)	4.63 (3.89-5.52, p<0.001)	6.26 (5.13-7.65, p<0.001)
Sex at Birth	Female	14550 (70.9)	5968 (29.1)	-	-
	Male	17230 (70.2)	7308 (29.8)	1.03 (0.99-1.08, p=0.107)	1.05 (1.01-1.10, p=0.021)
Deprivation	1 (least deprived)	4468 (69.7)	1946 (30.3)	-	-
	2	5473 (70.0)	2345 (30.0)	0.98 (0.92-1.06, p=0.655)	0.97 (0.90-1.05, p=0.442)
	3	6751 (69.4)	2983 (30.6)	1.01 (0.95-1.09, p=0.680)	1.03 (0.95-1.12, p=0.438)
	4	7008 (70.2)	2982 (29.8)	0.98 (0.91-1.05, p=0.504)	1.07 (0.99-1.16, p=0.095)
	5 (most deprived)	8156 (72.8)	3052 (27.2)	0.86 (0.80-0.92, p<0.001)	1.03 (0.95-1.11, p=0.545)

Supplementary table 10B - Systemic complications

Dependent: Self-care ability		Equivalent to before illness	Worse	OR (univariable)	OR (multilevel)
Systemic complication	No	26339 (73.7)	9378 (26.3)	-	-
	Yes	3812 (56.1)	2987 (43.9)	2.20 (2.09-2.32, p<0.001)	2.39 (2.25-2.53, p<0.001)
Age (years)	19-29	1121 (86.7)	172 (13.3)	-	-
	30-39	1962 (83.7)	383 (16.3)	1.27 (1.05-1.55, p=0.015)	1.66 (1.33-2.09, p<0.001)
	40-49	3331 (79.9)	838 (20.1)	1.64 (1.38-1.96, p<0.001)	2.28 (1.85-2.82, p<0.001)
	50-59	5508 (78.8)	1486 (21.2)	1.76 (1.49-2.09, p<0.001)	2.46 (2.01-3.02, p<0.001)
	60-69	5451 (73.3)	1990 (26.7)	2.38 (2.02-2.82, p<0.001)	3.36 (2.74-4.11, p<0.001)
	70-79	6237 (66.5)	3139 (33.5)	3.28 (2.79-3.88, p<0.001)	4.66 (3.82-5.69, p<0.001)
	80-89	6069 (61.4)	3810 (38.6)	4.09 (3.48-4.84, p<0.001)	6.03 (4.94-7.36, p<0.001)
	90+	1940 (58.5)	1377 (41.5)	4.63 (3.89-5.52, p<0.001)	6.99 (5.68-8.62, p<0.001)
Sex at Birth	Female	14550 (70.9)	5968 (29.1)	-	-
	Male	17230 (70.2)	7308 (29.8)	1.03 (0.99-1.08, p=0.107)	1.10 (1.05-1.15, p<0.001)
Deprivation	1 (least deprived)	4468 (69.7)	1946 (30.3)	-	-
	2	5473 (70.0)	2345 (30.0)	0.98 (0.92-1.06, p=0.655)	0.98 (0.91-1.07, p=0.687)
	3	6751 (69.4)	2983 (30.6)	1.01 (0.95-1.09, p=0.680)	1.03 (0.95-1.12, p=0.412)
	4	7008 (70.2)	2982 (29.8)	0.98 (0.91-1.05, p=0.504)	1.09 (1.01-1.19, p=0.031)
	5 (most deprived)	8156 (72.8)	3052 (27.2)	0.86 (0.80-0.92, p<0.001)	1.03 (0.95-1.12, p=0.429)

Supplementary table 10C - Renal complications/ acute kidney injury

Dependent: Self-care ability		Equivalent to before illness	Worse	OR (univariable)	OR (multilevel)
Renal complication	No	25847 (74.1)	9039 (25.9)	-	-
	Yes	5287 (58.2)	3791 (41.8)	2.05 (1.95-2.15, p<0.001)	2.12 (2.01-2.23, p<0.001)
Age (years)	19-29	1121 (86.7)	172 (13.3)	-	-
	30-39	1962 (83.7)	383 (16.3)	1.27 (1.05-1.55, p=0.015)	1.67 (1.34-2.10, p<0.001)
	40-49	3331 (79.9)	838 (20.1)	1.64 (1.38-1.96, p<0.001)	2.25 (1.83-2.77, p<0.001)
	50-59	5508 (78.8)	1486 (21.2)	1.76 (1.49-2.09, p<0.001)	2.38 (1.95-2.91, p<0.001)
	60-69	5451 (73.3)	1990 (26.7)	2.38 (2.02-2.82, p<0.001)	3.27 (2.68-3.99, p<0.001)
	70-79	6237 (66.5)	3139 (33.5)	3.28 (2.79-3.88, p<0.001)	4.45 (3.66-5.43, p<0.001)
	80-89	6069 (61.4)	3810 (38.6)	4.09 (3.48-4.84, p<0.001)	5.72 (4.70-6.97, p<0.001)
	90+	1940 (58.5)	1377 (41.5)	4.63 (3.89-5.52, p<0.001)	6.61 (5.38-8.13, p<0.001)
Sex at Birth	Female	14550 (70.9)	5968 (29.1)	-	-
	Male	17230 (70.2)	7308 (29.8)	1.03 (0.99-1.08, p=0.107)	1.06 (1.01-1.11, p=0.017)
Deprivation	1 (least deprived)	4468 (69.7)	1946 (30.3)	-	-
	2	5473 (70.0)	2345 (30.0)	0.98 (0.92-1.06, p=0.655)	0.97 (0.89-1.05, p=0.443)
	3	6751 (69.4)	2983 (30.6)	1.01 (0.95-1.09, p=0.680)	1.02 (0.94-1.11, p=0.590)
	4	7008 (70.2)	2982 (29.8)	0.98 (0.91-1.05, p=0.504)	1.06 (0.98-1.15, p=0.139)
	5 (most deprived)	8156 (72.8)	3052 (27.2)	0.86 (0.80-0.92, p<0.001)	1.01 (0.94-1.10, p=0.724)

Supplementary table 10D - Gastrointestinal and liver complications

Dependent: Self-care ability		Equivalent to before illness	Worse	OR (univariable)	OR (multilevel)
Gastrointestinal complication	No	29144 (71.4)	11650 (28.6)	-	-
	Yes	2722 (62.1)	1659 (37.9)	1.52 (1.43-1.63, p<0.001)	1.95 (1.82-2.10, p<0.001)
Age (years)	19-29	1121 (86.7)	172 (13.3)	-	-
	30-39	1962 (83.7)	383 (16.3)	1.27 (1.05-1.55, p=0.015)	1.57 (1.27-1.95, p<0.001)
	40-49	3331 (79.9)	838 (20.1)	1.64 (1.38-1.96, p<0.001)	2.14 (1.76-2.61, p<0.001)
	50-59	5508 (78.8)	1486 (21.2)	1.76 (1.49-2.09, p<0.001)	2.39 (1.97-2.89, p<0.001)
	60-69	5451 (73.3)	1990 (26.7)	2.38 (2.02-2.82, p<0.001)	3.37 (2.79-4.08, p<0.001)
	70-79	6237 (66.5)	3139 (33.5)	3.28 (2.79-3.88, p<0.001)	4.75 (3.94-5.73, p<0.001)
	80-89	6069 (61.4)	3810 (38.6)	4.09 (3.48-4.84, p<0.001)	6.14 (5.09-7.41, p<0.001)
	90+	1940 (58.5)	1377 (41.5)	4.63 (3.89-5.52, p<0.001)	7.12 (5.85-8.67, p<0.001)
Sex at Birth	Female	14550 (70.9)	5968 (29.1)	-	-
	Male	17230 (70.2)	7308 (29.8)	1.03 (0.99-1.08, p=0.107)	1.09 (1.04-1.14, p<0.001)
Deprivation	1 (least deprived)	4468 (69.7)	1946 (30.3)	-	-
	2	5473 (70.0)	2345 (30.0)	0.98 (0.92-1.06, p=0.655)	0.97 (0.90-1.05, p=0.470)
	3	6751 (69.4)	2983 (30.6)	1.01 (0.95-1.09, p=0.680)	1.05 (0.97-1.13, p=0.262)
	4	7008 (70.2)	2982 (29.8)	0.98 (0.91-1.05, p=0.504)	1.09 (1.01-1.18, p=0.023)
	5 (most deprived)	8156 (72.8)	3052 (27.2)	0.86 (0.80-0.92, p<0.001)	1.05 (0.97-1.13, p=0.272)

Supplementary table 10E - Cardiovascular complications

Dependent: Self-care ability		Equivalent to before illness	Worse	OR (univariable)	OR (multilevel)
Cardiovascular complication	No	28222 (72.7)	10600 (27.3)	-	-
	Yes	1957 (53.3)	1716 (46.7)	2.33 (2.18-2.50, p<0.001)	2.18 (2.02-2.35, p<0.001)
Age (years)	19-29	1121 (86.7)	172 (13.3)	-	-
	30-39	1962 (83.7)	383 (16.3)	1.27 (1.05-1.55, p=0.015)	1.69 (1.34-2.12, p<0.001)
	40-49	3331 (79.9)	838 (20.1)	1.64 (1.38-1.96, p<0.001)	2.26 (1.83-2.79, p<0.001)
	50-59	5508 (78.8)	1486 (21.2)	1.76 (1.49-2.09, p<0.001)	2.46 (2.00-3.01, p<0.001)
	60-69	5451 (73.3)	1990 (26.7)	2.38 (2.02-2.82, p<0.001)	3.34 (2.73-4.08, p<0.001)
	70-79	6237 (66.5)	3139 (33.5)	3.28 (2.79-3.88, p<0.001)	4.60 (3.77-5.62, p<0.001)
	80-89	6069 (61.4)	3810 (38.6)	4.09 (3.48-4.84, p<0.001)	5.91 (4.84-7.21, p<0.001)
	90+	1940 (58.5)	1377 (41.5)	4.63 (3.89-5.52, p<0.001)	6.74 (5.47-8.30, p<0.001)
Sex at Birth	Female	14550 (70.9)	5968 (29.1)	-	-
	Male	17230 (70.2)	7308 (29.8)	1.03 (0.99-1.08, p=0.107)	1.10 (1.05-1.15, p<0.001)
Deprivation	1 (least deprived)	4468 (69.7)	1946 (30.3)	-	-
	2	5473 (70.0)	2345 (30.0)	0.98 (0.92-1.06, p=0.655)	0.98 (0.90-1.06, p=0.554)
	3	6751 (69.4)	2983 (30.6)	1.01 (0.95-1.09, p=0.680)	1.03 (0.95-1.12, p=0.447)
	4	7008 (70.2)	2982 (29.8)	0.98 (0.91-1.05, p=0.504)	1.08 (1.00-1.18, p=0.051)
	5 (most deprived)	8156 (72.8)	3052 (27.2)	0.86 (0.80-0.92, p<0.001)	1.03 (0.95-1.12, p=0.507)

Supplementary table 10F - Neurological complications

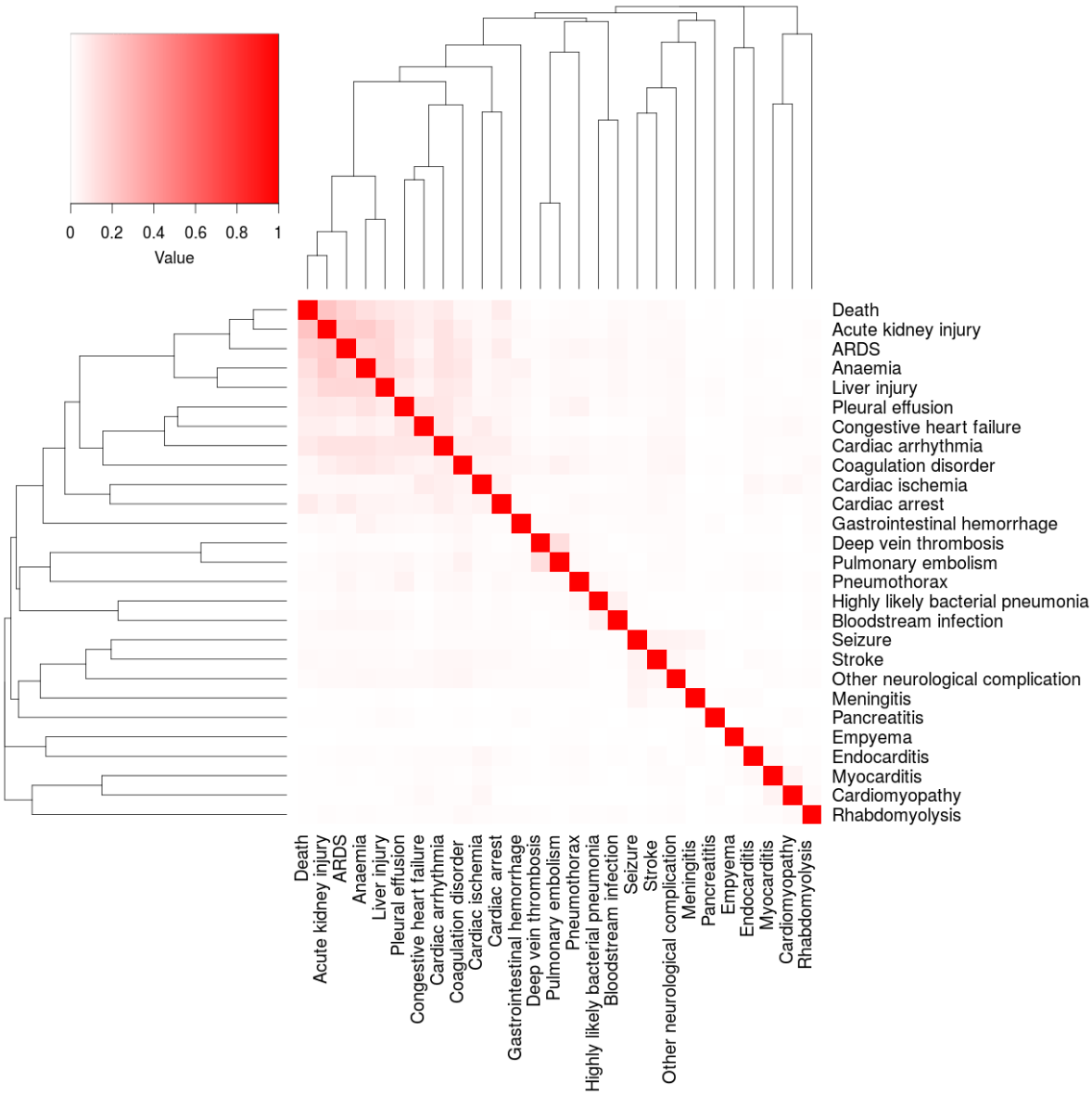
Dependent: Self-care ability		Equivalent to before illness	Worse	OR (univariable)	OR (multilevel)
Neurological complication	No	29467 (72.4)	11216 (27.6)	-	-
	Yes	645 (37.5)	1074 (62.5)	4.37 (3.96-4.84, p<0.001)	4.35 (3.90-4.84, p<0.001)
Age (years)	19-29	1121 (86.7)	172 (13.3)	-	-
	30-39	1962 (83.7)	383 (16.3)	1.27 (1.05-1.55, p=0.015)	1.68 (1.33-2.10, p<0.001)
	40-49	3331 (79.9)	838 (20.1)	1.64 (1.38-1.96, p<0.001)	2.27 (1.84-2.81, p<0.001)
	50-59	5508 (78.8)	1486 (21.2)	1.76 (1.49-2.09, p<0.001)	2.47 (2.02-3.03, p<0.001)
	60-69	5451 (73.3)	1990 (26.7)	2.38 (2.02-2.82, p<0.001)	3.41 (2.78-4.17, p<0.001)
	70-79	6237 (66.5)	3139 (33.5)	3.28 (2.79-3.88, p<0.001)	4.73 (3.87-5.78, p<0.001)
	80-89	6069 (61.4)	3810 (38.6)	4.09 (3.48-4.84, p<0.001)	6.08 (4.98-7.43, p<0.001)
	90+	1940 (58.5)	1377 (41.5)	4.63 (3.89-5.52, p<0.001)	6.97 (5.66-8.60, p<0.001)
Sex at Birth	Female	14550 (70.9)	5968 (29.1)	-	-
	Male	17230 (70.2)	7308 (29.8)	1.03 (0.99-1.08, p=0.107)	1.10 (1.05-1.15, p<0.001)
Deprivation	1 (least deprived)	4468 (69.7)	1946 (30.3)	-	-
	2	5473 (70.0)	2345 (30.0)	0.98 (0.92-1.06, p=0.655)	0.98 (0.91-1.07, p=0.681)
	3	6751 (69.4)	2983 (30.6)	1.01 (0.95-1.09, p=0.680)	1.04 (0.96-1.13, p=0.327)
	4	7008 (70.2)	2982 (29.8)	0.98 (0.91-1.05, p=0.504)	1.11 (1.02-1.20, p=0.015)
	5 (most deprived)	8156 (72.8)	3052 (27.2)	0.86 (0.80-0.92, p<0.001)	1.03 (0.95-1.12, p=0.465)

Supplementary table 10G - Respiratory complications

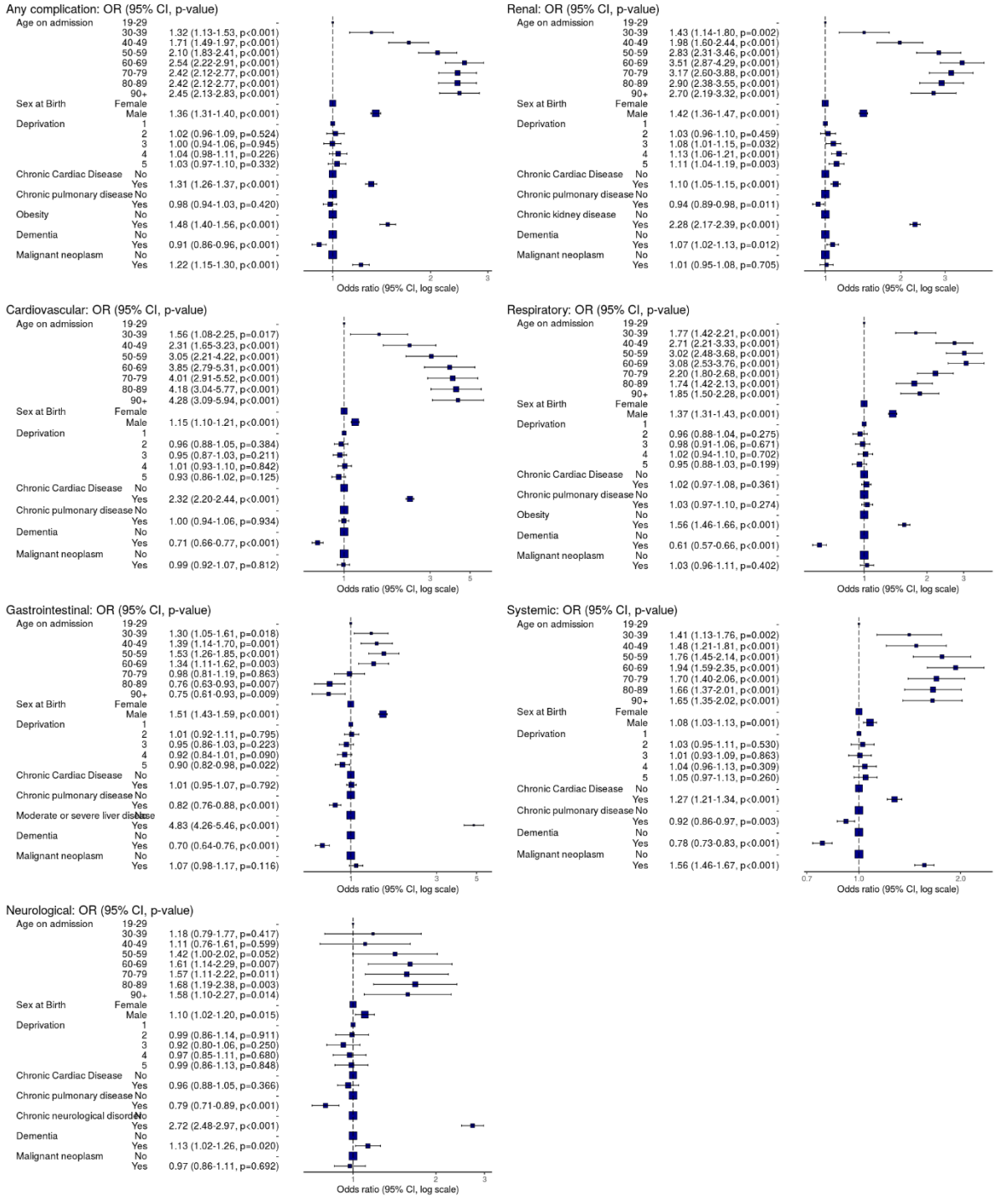
Dependent: Self-care ability		Equivalent to before illness	Worse	OR (univariable)	OR (multilevel)
Respiratory complication	No	26878 (74.2)	9360 (25.8)	-	-
	Yes	3380 (52.4)	3069 (47.6)	2.61 (2.47-2.75, p<0.001)	3.61 (3.39-3.84, p<0.001)
Age (years)	19-29	1121 (86.7)	172 (13.3)	-	-
	30-39	1962 (83.7)	383 (16.3)	1.27 (1.05-1.55, p=0.015)	1.58 (1.25-1.99, p<0.001)
	40-49	3331 (79.9)	838 (20.1)	1.64 (1.38-1.96, p<0.001)	2.02 (1.63-2.50, p<0.001)
	50-59	5508 (78.8)	1486 (21.2)	1.76 (1.49-2.09, p<0.001)	2.22 (1.80-2.72, p<0.001)
	60-69	5451 (73.3)	1990 (26.7)	2.38 (2.02-2.82, p<0.001)	3.24 (2.64-3.98, p<0.001)
	70-79	6237 (66.5)	3139 (33.5)	3.28 (2.79-3.88, p<0.001)	4.90 (4.00-6.00, p<0.001)
	80-89	6069 (61.4)	3810 (38.6)	4.09 (3.48-4.84, p<0.001)	6.63 (5.42-8.12, p<0.001)
	90+	1940 (58.5)	1377 (41.5)	4.63 (3.89-5.52, p<0.001)	7.59 (6.14-9.38, p<0.001)
Sex at Birth	Female	14550 (70.9)	5968 (29.1)	-	-
	Male	17230 (70.2)	7308 (29.8)	1.03 (0.99-1.08, p=0.107)	1.06 (1.02-1.11, p=0.009)
Deprivation	1 (least deprived)	4468 (69.7)	1946 (30.3)	-	-
	2	5473 (70.0)	2345 (30.0)	0.98 (0.92-1.06, p=0.655)	0.98 (0.90-1.06, p=0.614)
	3	6751 (69.4)	2983 (30.6)	1.01 (0.95-1.09, p=0.680)	1.03 (0.95-1.12, p=0.419)
	4	7008 (70.2)	2982 (29.8)	0.98 (0.91-1.05, p=0.504)	1.08 (1.00-1.17, p=0.062)
	5 (most deprived)	8156 (72.8)	3052 (27.2)	0.86 (0.80-0.92, p<0.001)	1.04 (0.96-1.13, p=0.366)

Supplementary Figures

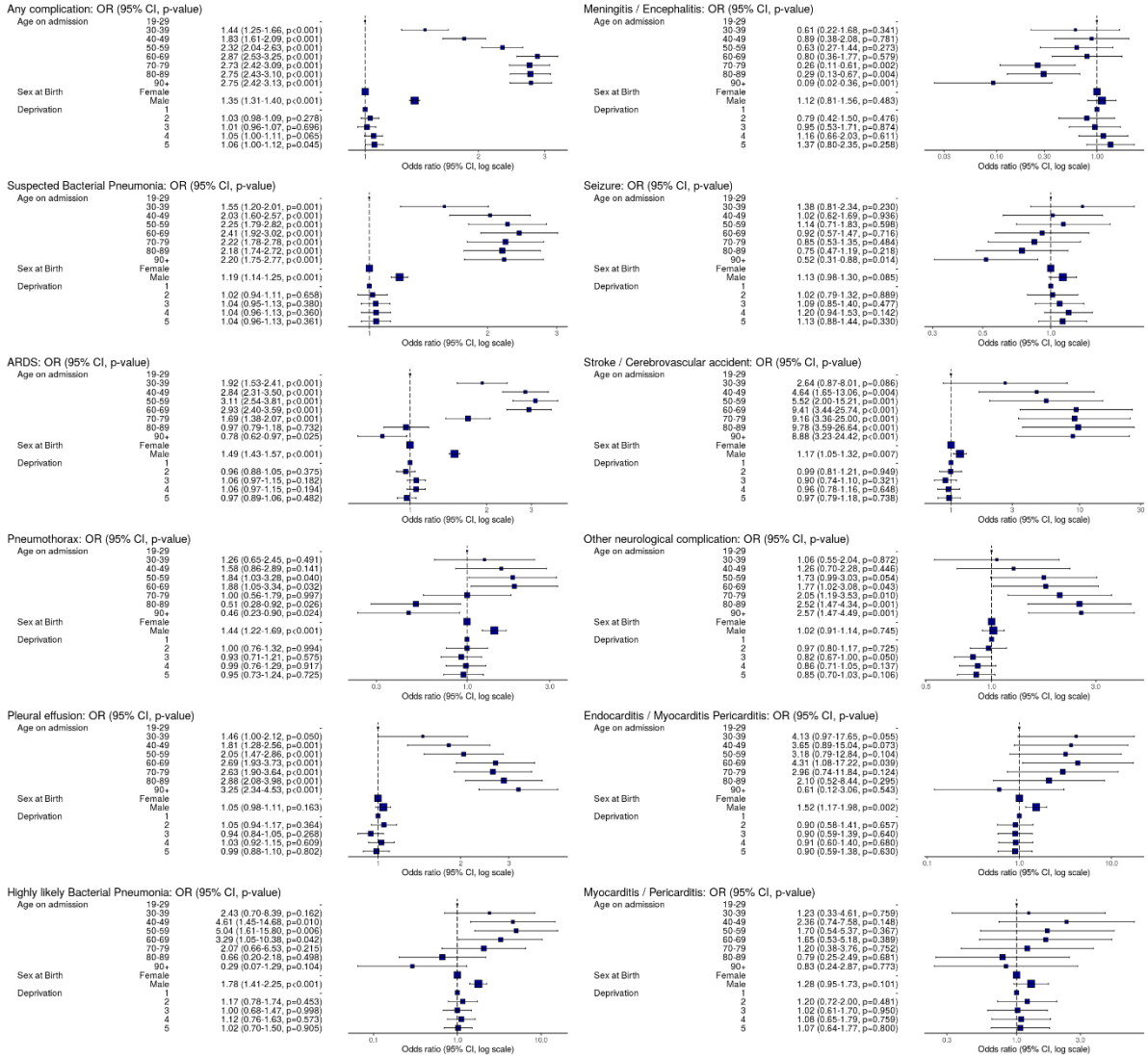
Supplementary figure 1 – Heatmap of co-occurence of complications. Measured using the Jaccard similarity index, where 1 is perfect co-occurrence and 0 is no co-occurrence.



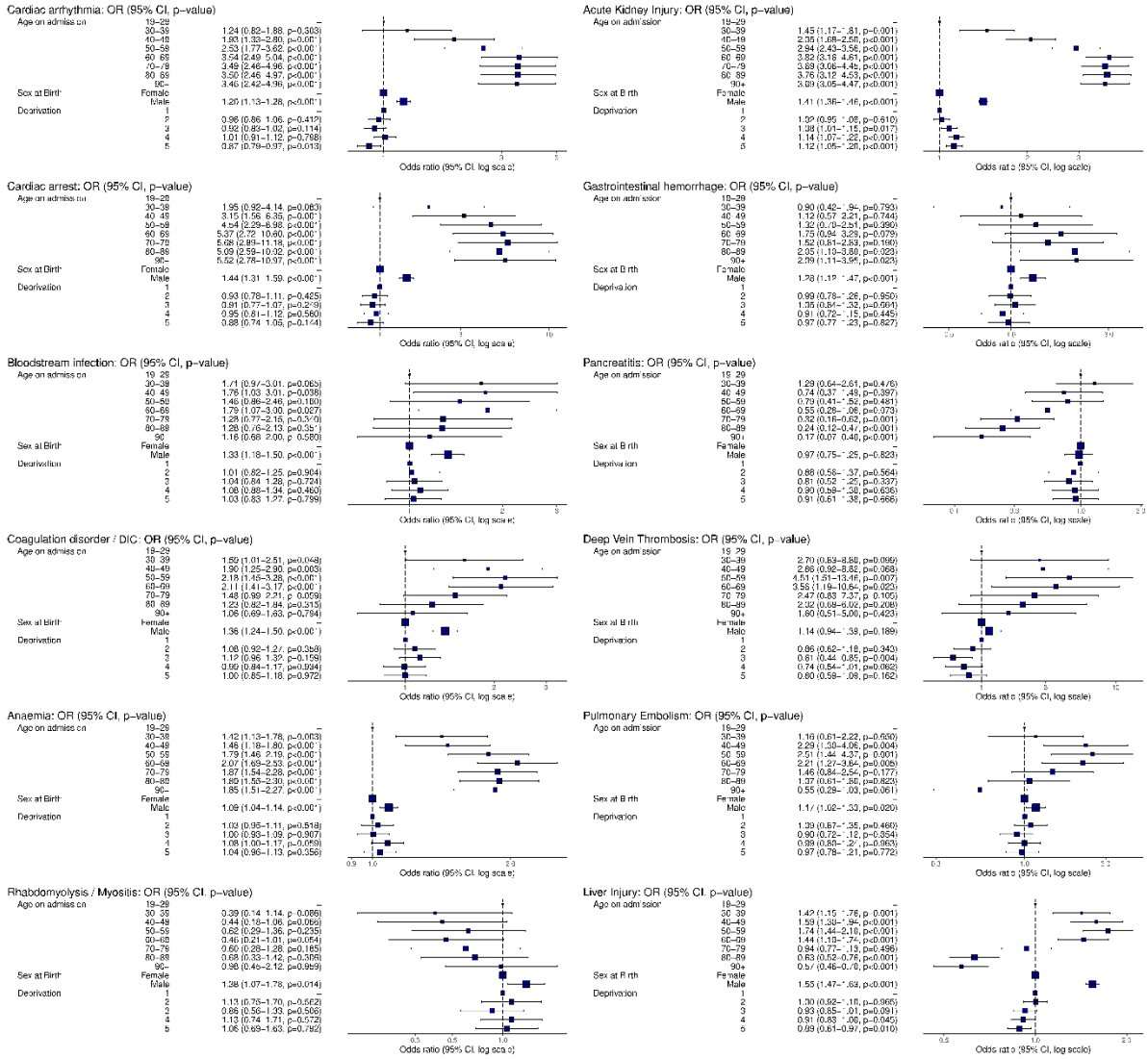
Supplementary figure 2 - Adjusted effect of age and sex on organ specific complications in adults with severe COVID-19 (also adjusted for centre as a random effect).



Supplementary figure 3 - Effect of age, sex and deprivation on specific complications in adults with COVID-19 (also adjusted for centre as a random effect).

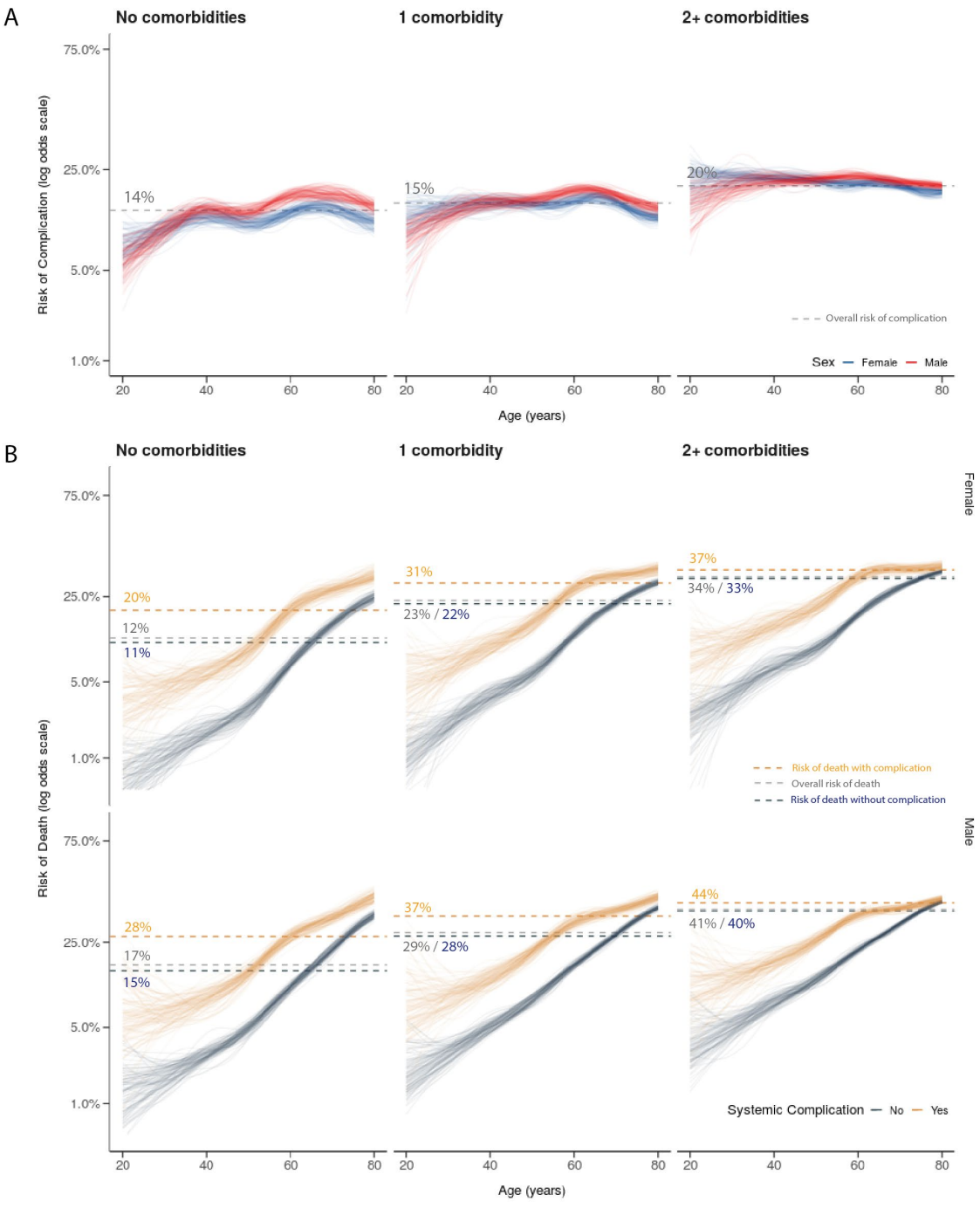


Supplementary figure 3 (continued) - Effect of age, sex and deprivation on specific complications in adults with COVID-19 (also adjusted for centre as a random effect).

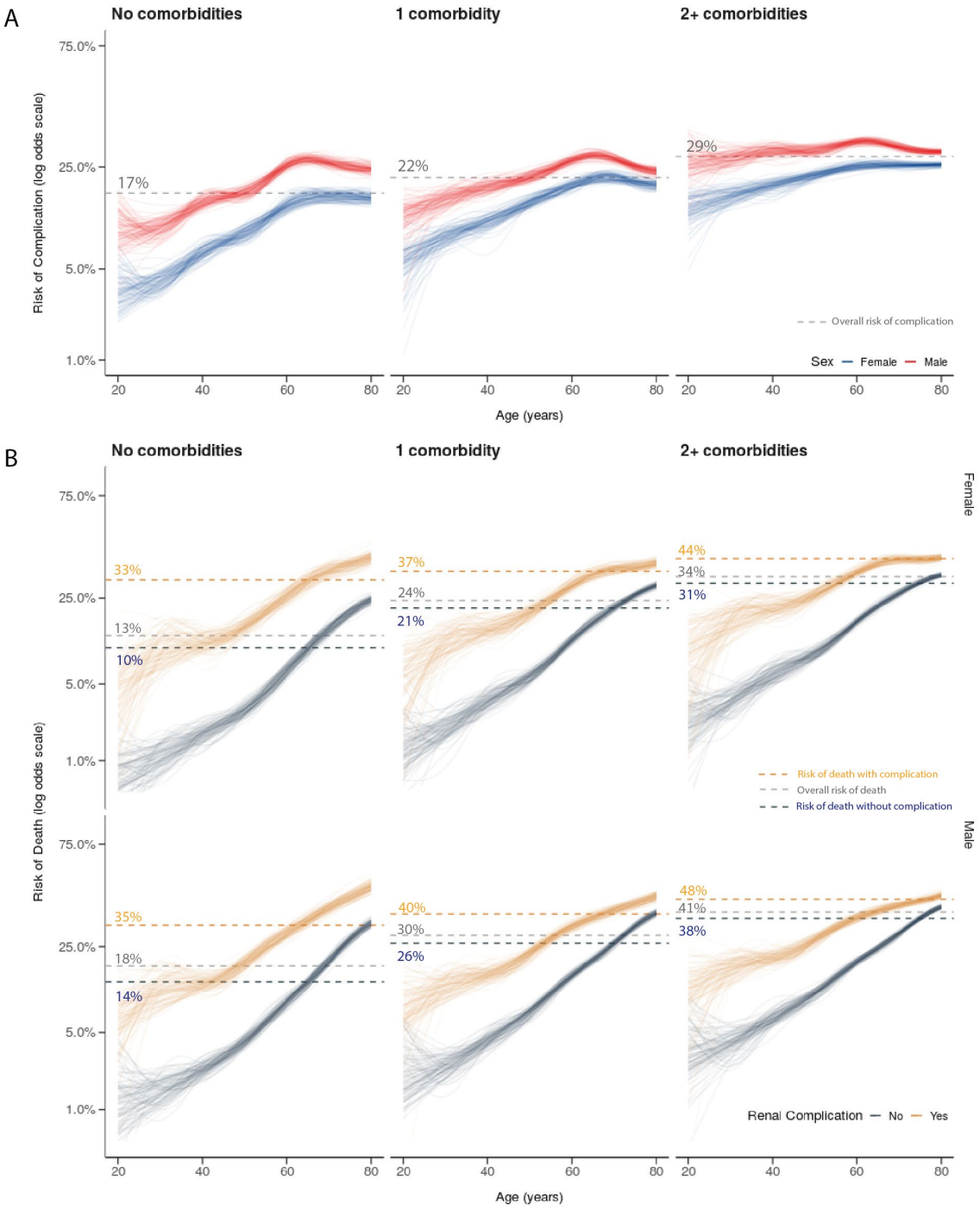


DIC- Disseminated intravascular coagulation.

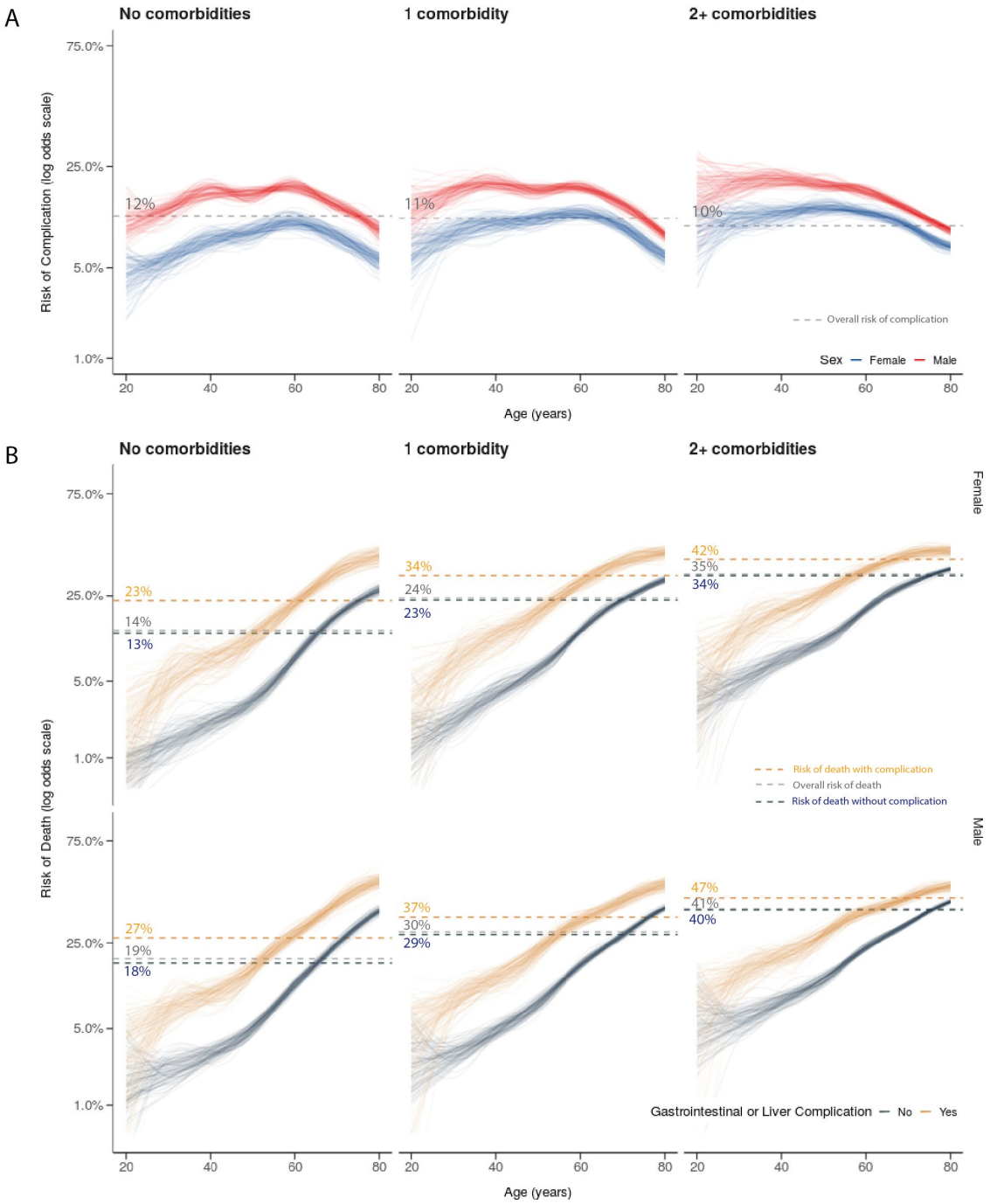
Supplementary figure 4 - Relationship between age, sex, comorbidities and adjusted outcomes using generalised additive models. (A) Shows relationships for the outcome of adjusted risk of systemic complications. (B) Shows relationships for the outcome of adjusted mortality risk, stratified by presence of systemic complications. Each line represents one bootstrap replicate (i.e. one simulated patient).



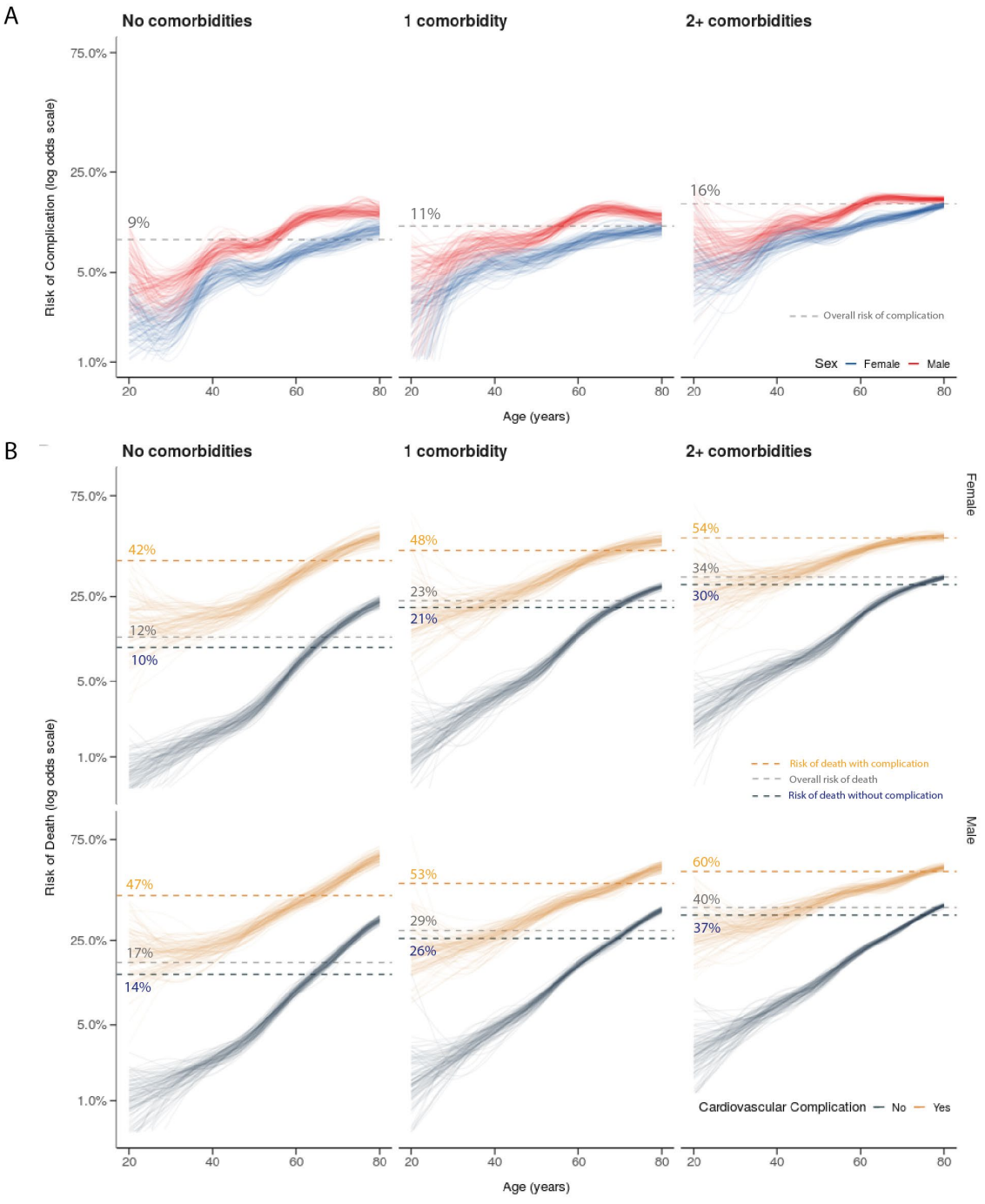
Supplementary figure 5 - Relationship between age, sex, comorbidities and adjusted outcomes using generalised additive models. (A) Shows relationships for the outcome of adjusted risk of renal complications. (B) Shows relationships for the outcome of adjusted mortality risk, stratified by presence of renal complications. Each line represents one bootstrap replicate (i.e. one simulated patient).



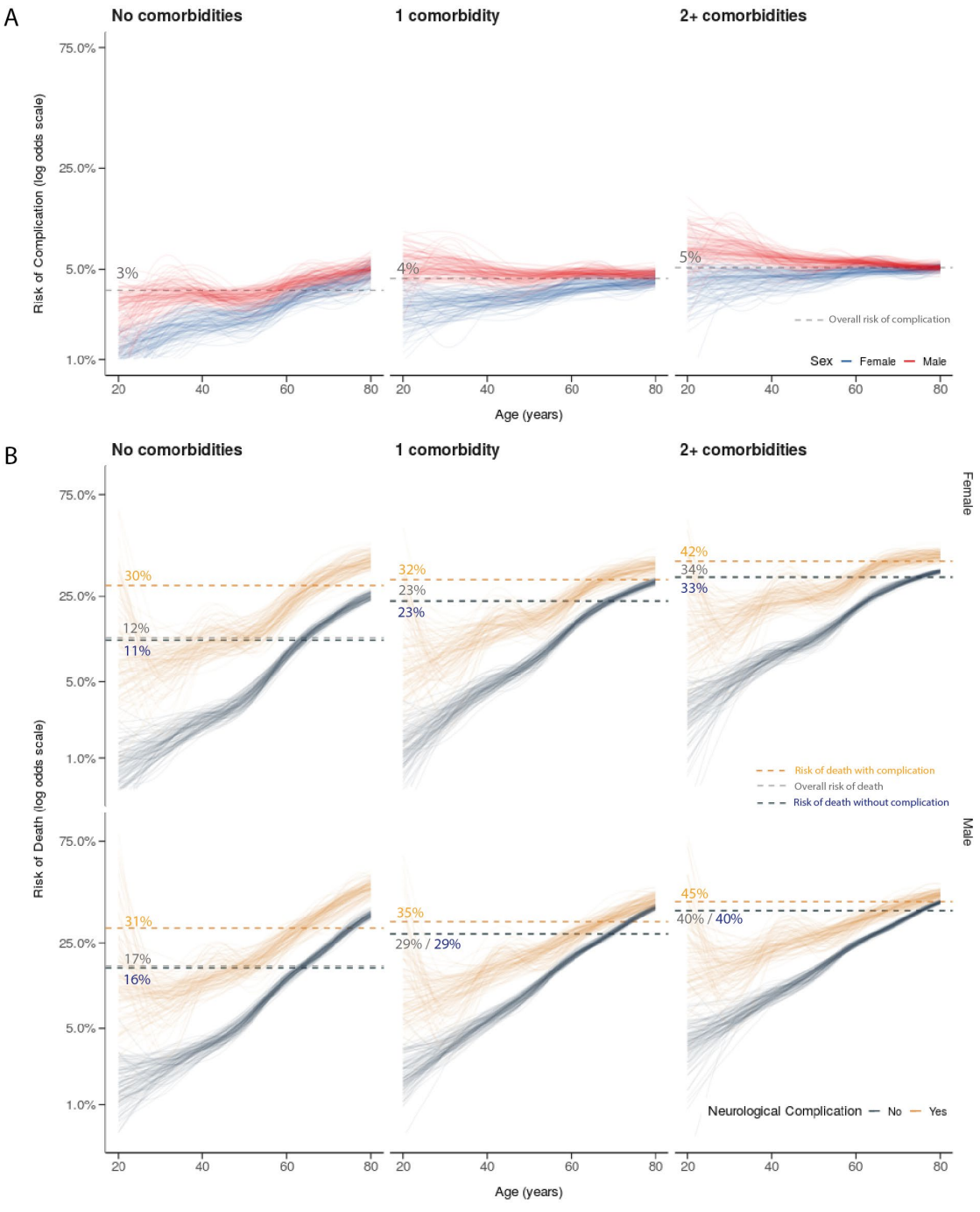
Supplementary figure 6 - Relationship between age, sex, comorbidities and adjusted outcomes using generalised additive models. (A) Shows relationships for the outcome of adjusted risk of gastrointestinal or liver complications. (B) Shows relationships for the outcome of adjusted mortality risk, stratified by presence of gastrointestinal or liver complications. Each line represents one bootstrap replicate (i.e. one simulated patient).



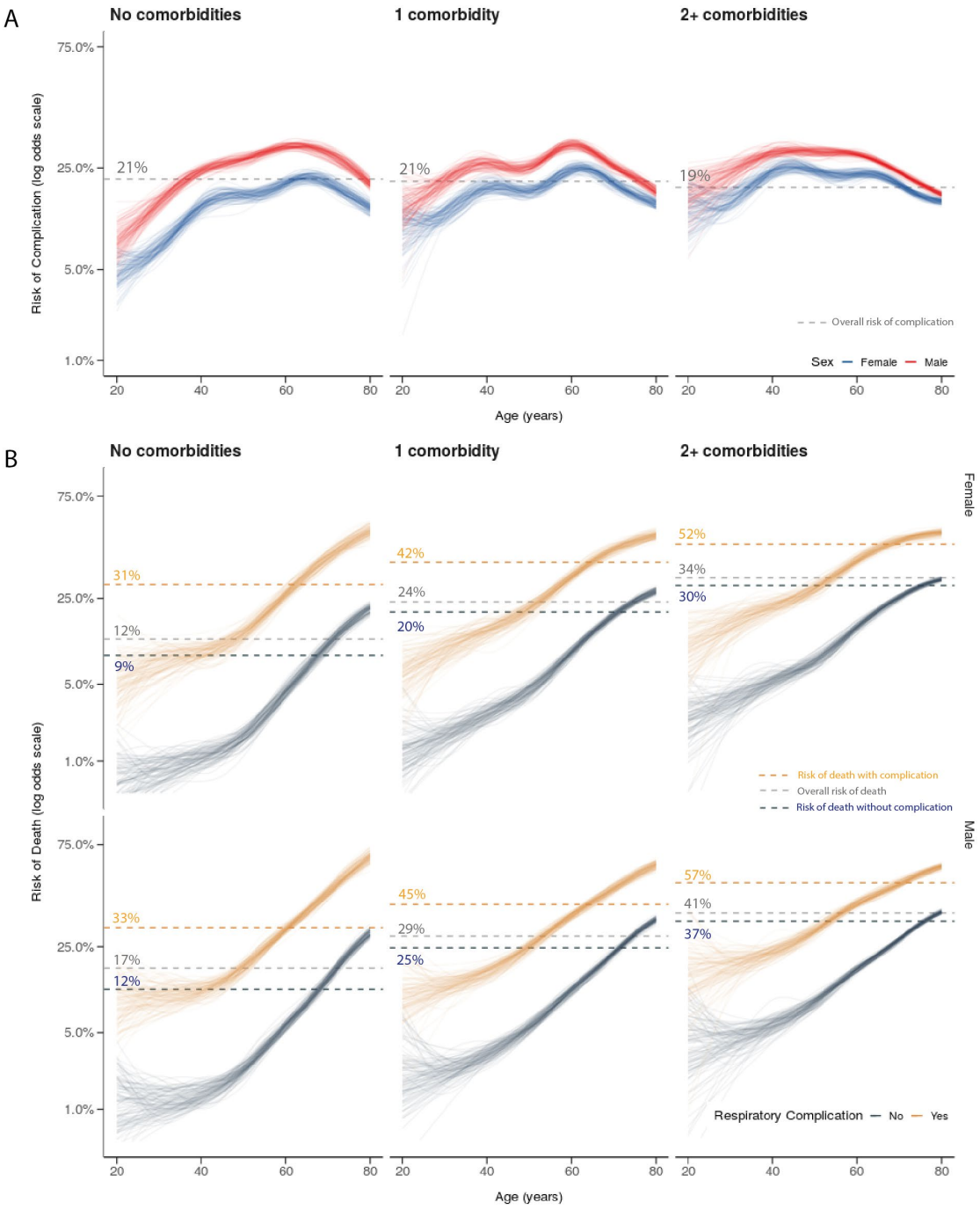
Supplementary figure 7 - Relationship between age, sex, comorbidities and adjusted outcomes using generalised additive models. (A) Shows relationships for the outcome of adjusted risk of cardiovascular complications. (B) Shows relationships for the outcome of adjusted mortality risk, stratified by presence of cardiovascular complications. Each line represents one bootstrap replicate (i.e. one simulated patient).



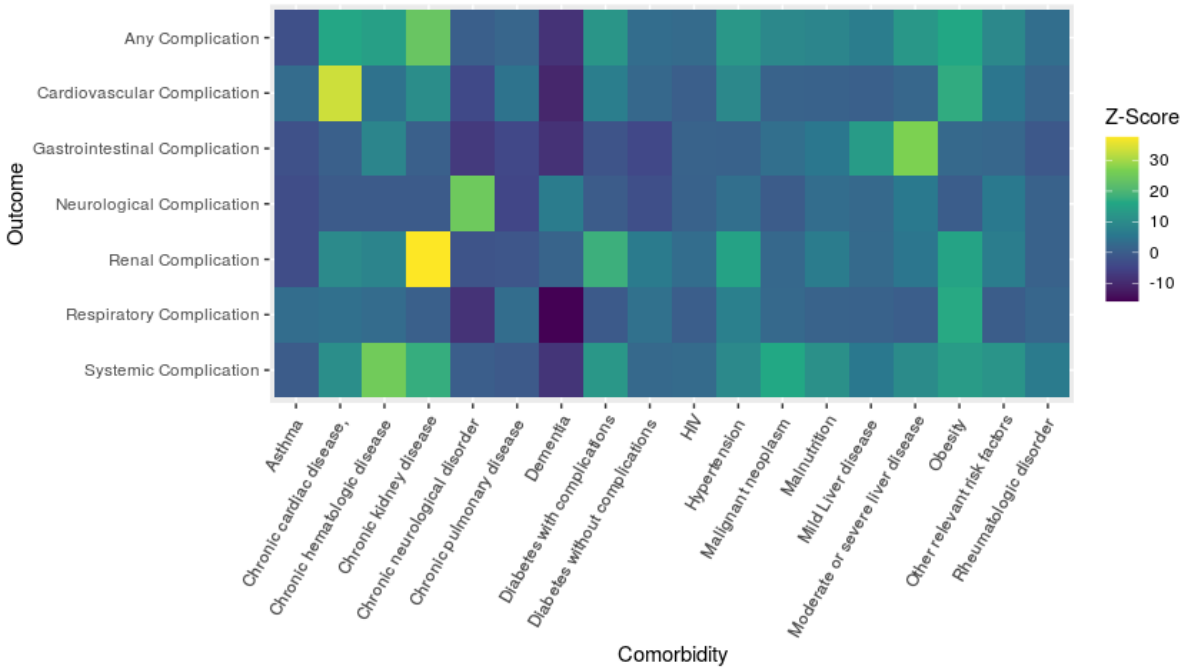
Supplementary figure 8 - Relationship between age, sex, comorbidities and adjusted outcomes using generalised additive models. (A) Shows relationships for the outcome of adjusted risk of neurological complications. (B) Shows relationships for the outcome of adjusted mortality risk, stratified by presence of neurological complications. Each line represents one bootstrap replicate (i.e. one simulated patient).



Supplementary figure 9 - Relationship between age, sex, comorbidities and adjusted outcomes using generalised additive models. (A) Shows relationships for the outcome of adjusted risk of respiratory complications. (B) Shows relationships for the outcome of adjusted mortality risk, stratified by presence of respiratory complications. Each line represents one bootstrap replicate (i.e. one simulated patient).

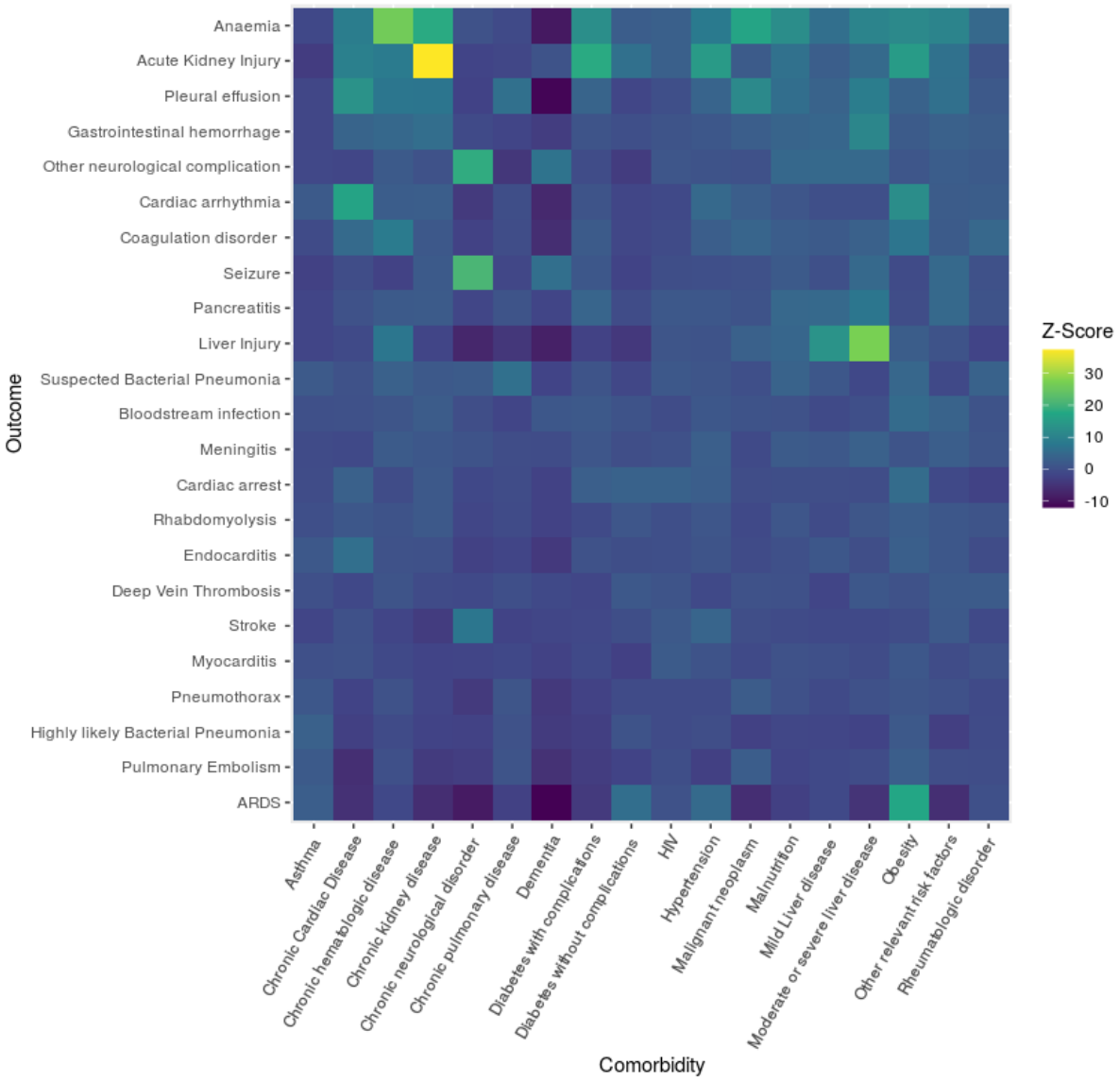


Supplementary figure 11 - Associations between specific comorbidities and organ specific complications in adults with severe COVID-19.



A positive Z-score represents stronger associations between variables in positive direction, whereas negative z-score represents effect in opposite direction.

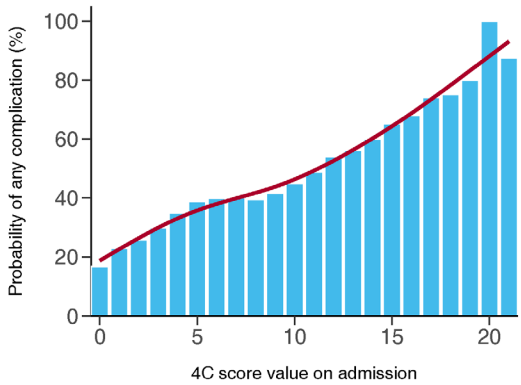
Supplementary figure 12 - Effect of specific comorbidities on specific complications in adults with COVID-19.



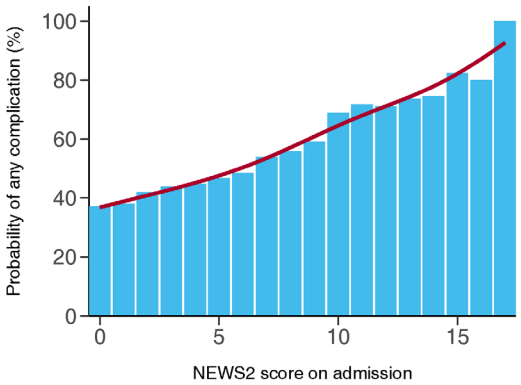
A positive Z-score represents stronger associations between variables in positive direction, whereas negative z-score represents effect in opposite direction.

Supplementary figure 13 – Probability of complication by admission severity score and symptoms in those who survived. (A) ISARIC 4C mortality score against proportion of patients experiencing any complication. (B) National Early Warning Score 2 against proportion of patients experiencing any complication. (C) Quick Sequential Organ Failure Assessment score against proportion of patients experiencing any complication. (D) Total number of symptoms on admission against proportion of patients experiencing any complication. For continuous outcomes (4C score, NEWS2 and number of symptoms), red line shows smoothed conditional mean line using generalised additive model. Higher scores indicate critical illness.

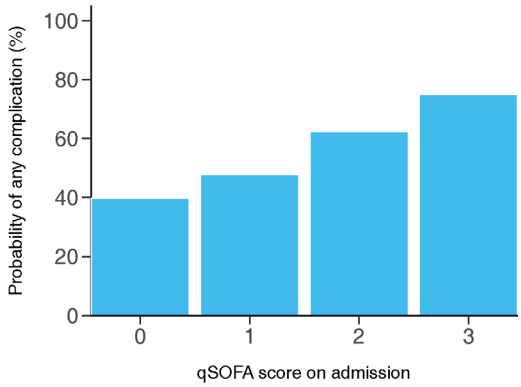
A



B



C



D